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The American Society of Tropical Medicine.

Papers Read Before the Society and Publishd Under Its Auspices.

Volume 1, 1904-1905.

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Articles of Association.

CHARTER.

Be it known that the subscribers, having associated themselves together for the purpose hereinafter mentioned, and being desirous of becoming incorporated agreeably to existing laws of the Commonwealth of Pennsylvania providing for the incorporation and regulation of certain corporations, approved April 29, 1874, and its supplements, do hereby declare and certify that the following are the purposes, objects, articles and conditions of their said association, for and on which they desire to be incorporated.

I. The name of the corporation shall be: AMERICAN SOCIETY OF TROPICAL MEDICINE.

II. The purpose for which the corporation is formed is to advance the knowledge of tropical diseases by encouraging original research by its members and others; collecting and recording facts ascertained by such researches, and disseminating information thereof by discussion among its members and by the publication of papers read before the society.

III. The corporation is to exist perpetually.

IV. The location of the Secretary's office shall be in the city of Philadelphia.

V. The names and residences of the subscribers hereto, are as follows: Thomas H. Fenton, M.D., 1319 Spruce St., Philadelphia; Judson Daland, M.D., 317 South 18th St., Philadelphia; Joseph McFarland, M.D., Medico-Chirurgical College, Philadelphia.

VI. The corporation is to be managed by a Council of five members, and a President and Secretary who shall be ex-officio members of the Council. In addition thereto there shall be annually chosen a Treasurer, two Vice-Presidents, and an Assistant Secretary. The names and residences of those chosen for the first year are: Thomas H. Fenton, M.D., Philadelphia, President; James C. Wilson, M.D., and James M. Anders, M.D., both of Philadelphia, Vice-Presidents; E. B. Gleason, M.D., Philadelphia, Treasurer; Joseph McFarland

M.D., Philadelphia, Secretary; John M. Swan, M.D., Philadelphia Assistant Secretary; and John V. Shoemaker, M.D., Hobart A. Hare, M.D., Roland G. Curtin, M.D., Judson Daland, M.D., Orville Horwitz, M.D., all of Philadelphia, Councillors.

VII. The Corporation has no capital stock.

American Society of Tropical Medicine.

BY-LAWS.

Recommended by Council at its meeting, March 20, 1903, and adopted May 25, 1903.

ARTICLE I.—The members of the Society shall be of three classes: *Active, Corresponding* and *Honorary.*

Any regular American physician interested in the study of tropical diseases, shall be eligible for *Active membership.*

Any regular physician not a resident of the United States, who has contributed to the knowledge of tropical diseases, shall be eligible for *Corresponding membership.*

Any scientist who has made eminent contributions to tropical medicine, shall be eligible for *Honorary membership.*

The number of active members shall be limited to 200. Candidates for membership shall be elected until 1904 by the Council, and thereafter by ballot at the annual meeting upon recommendation by the Council.

ARTICLE II.—The dues shall be fixed each year by the Council, but shall not be increased beyond $5.00 without approval by the Society at its annual meeting.

The regular dues shall be paid by active members only.

The corresponding and honorary members shall be exempt from dues.

ARTICLE III.—The officers shall consist of a President, two Vice-Presidents, a Treasurer, a Secretary, an Assistant Secretary, and a Council of five members. They shall perform the customary duties of such officers.

The Council shall have general supervision of the affairs of the Society, and shall meet from time to time as they determine. The President and Secretary shall be ex-officio members of the Council. In 1905, three Councillors shall be elected for two years and two Councillors for one year. Thereafter each Councillor shall be elected for two years. In case of death or resignation of any officer or Councillor of the Society, the Council shall be empowered to fill such vacancy until the next annual meeting.

ARTICLE IV.—There shall be an annual meeting and such other scientific or business meetings as the Council shall determine.

The annual meeting shall be known as the business meeting when the election of officers for the ensuing year shall be held and routine and other business transacted.

ARTICLE V.—These By-Laws may be amended by a two-thirds vote of the Society at its annual meeting as suggested by Council provided such amendment has been offered to the Council one month previously, and recommended by it. Due notice of such contemplated changes to be sent out with the announcement of the annual meeting.

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ELECTED AT THE ANNUAL MEETING, MARCH 24, 1905.

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Communications concerning the Society should be sent to the Secretary, Dr. Joseph McFarland, Medico-Chirurgical College, Philadelphia, or to the Assistant Secretary, Dr. John M. Swan, 3713 Walnut Street, Philadelphia.

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Dr. E. E. Trotter, Chief Quarantine Officer, Havana, Cuba.

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A BRIEF REVIEW OF THE ÆTIOLOGY OF YELLOW FEVER.

AN ADDRESS BEFORE THE AMERICAN SOCIETY OF TROPICAL MEDICINE.*

By JAMES CARROLL, M. D.,

HONORARY MEMBER OF THE AMERICAN SOCIETY OF TROPICAL MEDICINE; MEMBER OF THE SOCIETY OF AMERICAN BACTERIOLOGISTS; OF THE AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS; OF THE WASHINGTON ACADEMY OF SCIENCES; OF THE AMERICAN PUBLIC HEALTH ASSOCIATION, ETC.; FIRST LIEUTENANT AND ASSISTANT SURGEON, U. S. ARMY.

Mr. Chairman, and Gentlemen:

When I received the honor of an invitation to address you on the subject of the ætiology of yellow fever, I felt that the time at my disposal was much too short at this busy season to permit me to do justice to so vast a subject. Nevertheless, I shall endeavor to take up, seriatim, the various lines of thought and the succeeding steps in the investigations that have led to our present belief that natural, or non-experimental, yellow fever can be contracted only through the bite of the mosquito, and that filthy environment and intimate personal contact with yellow fever patients, their garments, secretions,

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* Delivered at the University of Pennsylvania, Philadelphia, January 11, 1904.

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ejecta and dejecta, can be wholly ignored in our attempts to suppress or control this disease, the mosquito being the only factor that is necessary to consider.

Yellow fever is strictly an American plague from which no country has suffered so severely as the United States, and few cities more often and more fearfully than Philadelphia. Her experiences are written indelibly in the pages of history by the hand of such men as Carey, Currie, Caldwell, the immortal Rush, and the classic La Roche, whose treatise on yellow fever is a monumental compendium of facts with the deductions of a brilliant mind.

At the present day when so much is known of the minute bodies (bacteria) that are the actual causes of many pathological conditions, a discussion of the ætiology of a disease necessarily involves consideration of the specific causative factor, when it can be demonstrated. Unfortunately, we are unable to specify or describe the causative agent in yellow fever, but the sole transmitting agent is now well known and acknowledged, and measures based upon this knowledge have been found sufficient for all practical purposes in preventing, controlling, and suppressing the disease.

In former times the occurrence of pestilential disease was attributed to a "malignant constitution of the atmosphere," and this belief was shared by Sydenham and taught by his follower, Rush. Malarial fevers and yellow fever presented many points of similarity that led to their being attributed to a common cause. Both were believed to originate in the vicinity of standing water, especially about wharves, stagnant pools, and marshes, for in such locations the cases were found to be most numerous. It was a matter of common observation that the severest epidemics of yellow fever usually followed heavy falls of rain that had been succeeded by an unusually high range of atmospheric temperature. This naturally led to the belief that the epidemics resulted from the condition of the atmosphere, which was assumed to be heavily charged with poisonous effluvia from decomposing vegetable or animal matter, and the disease was therefore believed to be of endemic origin. This theory was strongly opposed by many who were able to bring forward ample proof that, in some instances at least, epidemics resulted from importation of the disease. Similar differences of opinion arose upon the subject of its contagiousness or non-contagiousness and were the cause of many bitter controversies. The rapidity with which the disease spread on shipboard and in certain houses and localities, together with the fact that persons visiting infected vessels or houses frequently contracted the disease, indicated that it was directly contagious. On the other hand, there was equally good evidence to show that it was not contagious, for patients who were treated in the country or in hospitals located upon high ground seldom or never communicated the disease to others. By some it was concluded that yellow fever was not actually contagious, but that it might acquire that property under certain conditions. The disease continued to be surrounded by the same mystery and perplexity until about three years ago, when the demonstration of the part played by the mosquito in its transmission placed it in the list of easily controllable and preventible diseases. The unusual prevalence of mosquitoes during an epidemic of yellow fever has been recorded a number of times; among the earliest to make this observation were Dr. Benjamin Rush, of Philadelphia, in 1797; Dr. John Vaughan,[1] of Wilmington, Del., in 1802, and later Dr. Weightman,[2] of the U. S. army, at St. Augustine, Fla., in 1839; Dr. Wood,[3] at Centreville, Mass., and Dr. Barton,[4] at Clinton, La., in 1853. Dr. Rush remarked that " *mosquitoes abounded, as usual, in sickly seasons.*"[5] Dr. Vaughan, in his excellent, though brief, description of the epidemic outbreak at Wilmington, in the year 1802,[6] wrote in regard to the season and the prevalence of mosquitoes as follows: " The season became tropical in the middle of August. The weather, from being uncommonly cool, suddenly became extremely hot, varying from 80 to 90 degrees, with frequent gusts of rain and lightning. In the evenings of the 29th, 30th, and 31st, there were excessively violent thunder storms from the westward with torrents of rain. . . . Myriads of mosquitoes infested the lower parts of the town from July until frost, having gradually diffused themselves over the borough in September. The eldest of our inhabitants do not recollect this insect's being troublesome here

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[1] *Medical Repository,* New York, Vol. vi, 1803, p. 301.

[2] *An Essay on Yellow Fever,* B. B. Strobel, M. D., Charleston, S. C., 1840, p. 162.

[3] and [4] *Report of Sanitary Condition of New Orleans on the Epidemic of Yellow Fever of* 1853. New Orleans, 1854, Vol. 1, pp. 266, 278, 540.

[5] *Medical Inquiries and Observations.* Benjamin Rush, M. D., Philadelphia, 1805, Vol. iv, p. 77.

[6] *Medical Repository,* New York, Vol. vi, 1803, p. 301.

in any previous season; while the unanimous report of persons from the fenny counties of Kent and Sussex, the annual haunts of these winged pests, was that they were unusually free from them." Please note the occurrence of heavy rains which were followed by unusually high temperature, making conditions most favorable for the propagation of mosquitoes. Similar conditions of moisture accompanied or followed by unusually high temperature have been recorded as preceding epidemics of yellow fever by scores of American writers, some of whom observed also that these conditions were not necessarily accompanied by epidemics. Observe, also, that mosquitoes infested the lower parts of the town until frost; that these insects had not been troublesome before within the recollection of the oldest inhabitants, and that adjacent marshy counties were unusually free from them. This would seem to render the inference justifiable that mosquitoes of the genus *Stegomyia* had been imported upon a vessel, and finding the conditions favorable they multiplied rapidly and diffused themselves throughout the lower parts of the town. Dr. Vaughan noted, also, that the progress of the infection was terminated by a single frost, and that the disease was not communicated to the attendants upon the sick, *when out of the original sphere of infection.*

I ask permission to refer briefly to the memorable epidemic of 1793, in this city, at the time when it was the capital of the nation. Its population then is said to have been forty thousand, of whom twelve thousand, or thirty per cent., fled to other places, and four thousand, or ten per cent. of the total population, died. The conditions are said to have rivaled those of European cities during the prevalence of the bubonic plague. The streets were deserted, friends no longer shook hands in greeting, and it was almost impossible to secure burial for the dead. Husbands deserted their wives and wives their husbands; parents forsook their children; masters turned their servants adrift or consigned them to the hospital; servants abandoned humane masters in their hour of greatest need, and, in some instances, those of affluent fortune who had given employment and sustenance to hundreds were turned over to the care of a mercenary negro, after their wives, children, friends, and servants had fled and left them to their fate.[7] On the other hand, there were innumerable instances of noble, self-sacrificing devotion to humanity. This was especially noted among the physicians, who, with few exceptions, remained at their posts and ministered to the sick. Within five or six weeks no less than ten physicians were carried away by the disease, and at one time, according to Dr. Rush, there were but three able to do duty out of their houses.[8] In the following year the city was again afflicted, and in writing of this epidemic, Dr. Rush says:[9] "As I considered the filth of the gutters and the stagnating water in the neighborhood of the city to be the remote causes of this fever, I advised the committee to have them both removed, and thereby to prevent the spreading of the disorder." It is evident from this that he had observed a close relationship between the prevalence of the fever and the presence of standing water; we know also that he afterwards remarked upon the presence of an unusual number of mosquitoes. To-day we have only gone a single step further in proving that the aerial connection between the stagnant water and the disease is by means of the mosquito instead of through the products of decomposition.

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[7] La Roche, *Yellow Fever,* Vol. i, p. 72.

[8] La Roche, *Yellow Fever,* Vol. i, p. 73.

[9] *Medical Inquiries and Observations,* by Benjamin Rush, M. D., Philadelphia, 1796, Vol. iv, p. 8.

After publication of the brilliant results of Koch and Pasteur, bacteriologists naturally looked upon yellow fever as affording a promising field for investigation. The first to enter the field was Dr. Domingos Freire, of Rio de Janeiro, who, in 1883, concluded that he had discovered the specific cause in an organism which he named the *Cryptococcus zanthogenicus.* He proceeded to inoculate human beings with attenuated cultures for the purpose of conferring immunity, and reported such favorable results, that in the same year he received a grant from the State to aid him in his work. He continued to report remarkably successful results in the way of protection conferred, and his inoculations were kept up until 1897. The work of Freire attracted considerable attention and, in 1887, Dr. Sternberg, of the United States army, was sent to Rio de Janeiro, for the purpose of investigating into and reporting upon the merits of these inoculations. The report of Sternberg was not favorable, for he found that a culture handed him by Dr. Freire did not agree with that investigator's description of his organism, and proved to be a common white staphylococcus.[10] Nevertheless, in Volume xx of the *Twentieth Century Practice of Medicine,* published in 1900,[11] we find no less than nine pages devoted to a consideration of Freire's work.

Dr. Carmona y Valle, of Mexico, published, in 1885, a description of an organism that he regarded as the cause of yellow fever; and Dr. Carlos Finlay, in Havana, attributed the same rôle to a *Micrococcus tetragenus,* with which he experimented on animals for some time, and to which, judging from his conversation, he was still inclined to attach some importance as late as 1901. Both these claims were disposed of by Sternberg, who showed that the bacteria described were common organisms that could be obtained from various sources. In 1889, Sternberg began a laborious study of the blood and organs from yellow fever cases in Havana. His examination included the intestinal contents and in his final report he stated that the specific infectious agent had not been demonstrated. There is good reason to believe that if the organism were capable of demonstration he would have found it, for his studies of the blood, tissues, and cultures obtained were of the most painstaking character and the methods employed by him were but little inferior to those in use to-day.

In 1897, Dr. Sanarelli, a well known bacteriologist, announced his discovery of the specific agent of yellow fever in the form of a small bacillus, which he named *Bacillus icteroides.* After making a large number of experimental inoculations in animals, he announced that the clinical course of the infection produced by it was similar to that of yellow fever, and the lesions found *post mortem* were those of that disease. He also performed inoculations upon human beings and asserted that the clinical course and symptoms that followed were those of yellow fever. Sanarelli obtained his bacillus from about fifty per cent. of his cases, and stated[12] that he had never met with *Bacillus icteroides* alone; it was at least associated with the colon bacillus, staphylococcus, or streptococcus. Sanarelli's bacillus, however, differs in no respect from the paratyphoid or paracolon bacillus, the bacillus of hog cholera, Gaertner's *Bacillus enteritidis, Bacillus typhi murium,* and many others of the same group, except that it was obtained from a different source. If Sanarelli had been familiar with the hog cholera bacillus he would have had no difficulty in identifying his *Bacillus icteroides,* for in all their characteristics, both morphological and biological, these organisms are identical. In 1897, at the instigation of Surgeon-General G. M. Sternberg, U. S. army, Dr. Reed and the writer began their work with bacillus X and *Bacillus icteroides.*[13] We succeeded later in producing all the lesions and symptoms of acute hog cholera in young hogs by feeding them with pure cultures of Sanarelli's bacillus. We found that cultures of *Bacillus icteroides,* when injected into rabbits, guinea pigs, mice, dogs, and pigeons, produced similar infections and the same pathological lesions as the bacillus of hog cholera, and further, that the blood of dogs rendered immune against either of these organisms gave reciprocal agglutinative reactions.[14] In a recent publication of the U. S. Department of Agriculture, Mohler and Buckley[15] give an excellent description of an organism of this group obtained from cattle during an outbreak of septicæmia. When given to hogs it produced the symptoms and lesions of acute hog cholera. They proved its close relationship to *Bacillus paracolon,* and it is apparent that it could with equal propriety be designated the bacillus of Gaertner, paracolon, or, hog cholera bacillus. It is now well established that bacilli of this group have a wide range of pathogenicity, having been isolated under various names from cattle, hogs, ferrets, mice, birds, and human beings. Obtained from the latter source they are known as Gaertner's bacillus, paratyphoid or paracolon bacillus, and *Bacillus icteroides.* As an illustration of their close relationship and probable identity I can cite the testimony of Dr. Joseph McFarland, the secretary of this society, who, during the early period of our work, wrote to Dr. Reed for a culture of *Bacillus icteroides,* which was sent to him. A few weeks later he again wrote to Dr. Reed accusing him of playing a joke and of sending a culture of the hog cholera bacillus instead of *Bacillus icteroides.* These organisms are widely distributed in Nature, in man and animals; I have isolated them from spring water where the chances of contamination were very remote. Although certain minor variations, such as size and appearance of the colonies, mobility, etc., may appear in the comparative study of these various bacilli, all these variations become reconciled if one studies a number of cultures of genuine hog cholera bacilli. I might mention here that a paratyphoid bacillus isolated by Dr. Harvey Cushing,[16] of Baltimore, which he called Bacillus O, was agglutinated by Sanarelli's antiamaryllic serum (prepared with *Bacillus icteroides*) in very high dilution (1-30,000). This serum was intended for use in the treatment of cases of yellow fever. A similar result was also obtained with cultures of the hog cholera bacillus, using a dilution of 1-10,000. Sanarelli's observations were confirmed by a number of observers, among them Wasdin and Geddings, of the Marine Hospital Service, who reported[17] that they had infected monkeys, dogs, rabbits, guinea pigs, rats, and mice with yellow fever by inoculation with cultures of *Bacillus icteroides.* They also found that certain of these animals could be infected by insufflation of dried cultures, and concluded that in yellow fever infection took place by way of the respiratory tract through primary colonization in the lungs.

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[10] *Report on the Ætiology and Prevention of Yellow Fever,* by George M. Sternberg. Washington, Government Printing Office, 1890.

[11] *Twentieth Century Practice of Medicine,* New York, Vol. xx, pp. 452 to 461.

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[12] Lecture delivered before the University of Montevideo, January 10, 1897, *British Medical Journal,* 1897, iii, p. 7.

[13] Reed and Carroll, The Specific Cause of Yellow Fever, *Medical News.* September 9, 1899.

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[14] Reed and Carroll, *Journal of Experimental Medicine,* Vol. v, No. 3, December 15, 1900.

[15] *Nineteenth Annual Report of the Bureau of Animal Industry,* 1902, p. 297.

In 1898, Dr. Aristides Agramonte, acting assistant surgeon, U. S. army, was assigned to duty in our laboratory for some months, for the purpose of studying *Bacillus icteroides* and bacillus X. He was then ordered to Cuba, where he succeeded in isolating *Bacillus icteroides* from about thirty-three per cent. of yellow fever cadavers examined at Santiago. He also obtained the organism from cases that were not yellow fever and concluded that it bore no relation to the disease.[18]

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[16] *Johns Hopkins Hospital Bulletin,* Nos. 112 to 113, July-August, 1900, p 156.

[17] *Report of the Commission of Medical Officers detailed by authority of the President to investigate the Cause of Yellow Fever.* Washington, Government Printing Office, 1899.

Early in 1900, yellow fever appeared among the American troops at Havana, and during the summer it became quite prevalent among the Americans and Spaniards in and about the city. In order to take the advantage of the opportunity offered for continuing the study of the ætiology of the disease, a board of army medical officers was ordered to meet at Havana for the purpose. It was composed of Major Walter Reed, surgeon, U. S. army, the writer, and Dr. Jesse M. Lazear, non-immunes, and Dr. Aristides Agramonte, a Cuban immune. The three last named were contract surgeons. Dr. Agramonte and Dr. Lazear were already on the island; Dr. Reed and the writer arrived at Havana, June 25, 1900, and within a day or two the board was organized and work begun. Cultures from the blood of eighteen patients drawn during life were carefully studied, and from these, as well as from cultures made at eleven autopsies, the board failed to recover *Bacillus icteroides;* the conclusion was drawn, therefore, that the organism could be excluded from further consideration. Two separate lines of work now presented; one, the study of the bacterial flora of the intestine and anaerobic cultures from the blood and various organs; the other, the theory of the transmission of the disease by the mosquito, which had been advanced by Dr. Carlos Finlay, in 1881. After due consideration it was decided to investigate the latter first, for various reasons: First, it seemed probable that it could be decided in a few weeks; second, there were many points of similarity between the two diseases, malaria and yellow fever, in regard to seasonal prevalence, favorable locality, manner of extension, etc.; third, the lapse of an interval of several weeks between primary and secondary cases pointed to the existence of an intermediate host; the prompt subsidence of an epidemic upon the occurrence of severe frosts corresponded with the effect of the latter upon the mosquito, and the same insect was suggested by the peculiar manner in which the disease appeared to jump from house to house, even when the inhabitants did not communicate with one another. Then arose the question of the tremendous responsibility involved in the use of human beings for experimental purposes. It was concluded that the results themselves, if positive, would be sufficient justification of the undertaking. It was suggested that we subject ourselves to the same risk, and this suggestion was accepted by Dr. Reed and Dr. Lazear. It became necessary for Dr. Reed to return to the United States, and the work was begun by Dr. Lazear, who applied infected mosquitoes to a number of persons, himself included, without result. On the afternoon of July 27, 1900, I submitted myself to the bite of an infected mosquito applied by Dr. Lazear. The insect, which had been hatched and reared in the laboratory, had been caused to feed upon four cases of yellow fever, two of them severe, and two mild. The first patient, a severe case, was bitten twelve days before; the second, third, and fourth patients had been bitten six, four, and two days previously, and were in character mild, severe, and mild, respectively. In writing to Dr. Reed that night of the incident I remarked jokingly that if there were anything in the mosquito theory I should have a good dose. And so it happened. After having slight premonitory symptoms for two days I was taken sick on August 31st, and on September 1st I was carried to the yellow fever camp. My life was in the balance for three days and my chart shows that on the fifth, sixth, and seventh days my urine contained eight tenths and nine tenths of moist albumin.[19] The tests were made by Dr. Lazear. I mention this particularly because the result obtained in this case does not agree with the twentieth conclusion of Marchoux, Salimbeni, and Simond,[20] that the longer the interval that elapses after infection of the mosquito the more dangerous he becomes. Twelve days, the period above cited, is the shortest time in which the mosquito has been proved to be capable of conveying the infection. It is my opinion that the susceptibility of the individual bitten is a much more potent factor in determining the severity of an attack than the duration of the infection in the mosquito, or the number of mosquitoes applied. On the day that I was taken sick, August 31, 1900, Dr. Lazear applied the same mosquito, with three others, to another individual who suffered a comparatively mild attack and was well before I had left my bed. It so happened that I was the first person in whom the mosquito was proved to convey the disease.

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[18] Aristides Agramonte. Report of Bacteriological Investigations upon Yellow Fever. *Medical News,* Vol. lxxvi, No. 6, 1900, p. 203 *et seq.,* and *Zentralblatt für Bakt.,* etc., Band xxv, Nos. 18-19, 1899.

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[19] The Ætiology of Yellow Fever,—A Preliminary Note. Reed, Carroll, Agramonte. and Lazear. *Proceedings of the Twenty-eighth Annual Meeting of the American Public Health Association, at Indianapolis, Ind.* Chart, Case I.

[20] *Annales de l'Institut Pasteur,* Tome xvii, No. 11, November, 1903, p 665.

On the eighteenth of September, five days after I was permitted to leave my bed, Dr. Lazear was stricken, and died in convulsions just one week later, after several days of delirium with black vomit. Such is yellow fever. He was bitten by a stray mosquito while applying other insects to a patient in one of the city hospitals. He did not recognize it as *Stegomyia* and thought it was a *Culex*. It was permitted to take its fill, and he attached no importance to the bite until after he was taken sick, when he related the incident to me. I shall never forget the expression of alarm in his eyes when I last saw him alive in the third or fourth day of his illness. The spasmodic contractions of his diaphragm indicated that black vomit was impending, and he fully appreciated their significance. The dreaded vomit soon appeared; I was too weak to see him again in that condition, and there was nothing I could do to help him. Dr. Lazear left a wife and two young children, one of whom he had never seen.

To Dr. Carlos Finlay, of Havana, belongs the credit for advancing the mosquito theory of the transmission of yellow fever. Soon after the announcement in England of Dr. Patrick Manson's discovery, that the mosquito served as the intermediary host for filariæ, Dr. Finlay conceived the idea that the same insect served as the intermediate bearer of the parasite of yellow fever. He began his attempted inoculations with the mosquito in June, 1881, and continued the work for a number of years, applying mosquitoes to one hundred persons. Of these, thirteen suffered attacks of yellow fever after periods varying from two to twenty-five days from the time they were bitten. Only three came down within the usual period of incubation. In no single instance could the attack that followed have been the result of the experimental application of the mosquito, because these insects when applied had been kept only from two to five days after biting a patient. In a single exception the insect had been kept six days. The four cases in which yellow fever developed within seven days were bitten, in Havana, at a time when yellow fever was epidemic in that city, and the mortality rate was high. I have been severely criticized by my Cuban friends for the statements I have already made in this connection,[21] and on sentimental grounds only; I still adhere to them, for I believe the facts as stated to be true, and they are of some historic interest. In the recently published report of the yellow fever commission of the Pasteur Institute the conclusion is reached that the infected mosquito is not dangerous until after the lapse of at least twelve days from the time she ingests the virulent blood.[22]

In December, 1900, under the direction of Dr.

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[21] The Transmission of Yellow Fever. James Carroll. *Journal of the American Medical Association,* May 23, 1903.

[22] Marchoux, Salimbeni, et Simond, *Annales de l'Institut Pasteur,* Tome xvii, No. 11, November, 1903.

Reed, an experimental station (Camp Lazear) was established in a secluded spot one mile from Columbia Barracks. Two thoroughly mosquito-proof buildings were constructed about eighty yards apart, one to be used for experiments with fomites, the other to demonstrate that an infected house could only be one that contained infected mosquitoes. The camp was placed under strict quarantine, the occupants were required to sleep beneath mosquito nets, and all precautions were taken to guard against introduction of the infection. The first successful experiment was made in the mosquito house, which was tightly sealed and had been divided by a complete wire screen partition into two compartments, each with a separate entrance. Into one of these compartments fifteen contaminated mosquitoes were turned loose and a non-immune entering the room three times on the same day was bitten fifteen times. Within four days he was down with yellow fever. Two other non-immunes who slept for thirteen nights in the other compartment, separated from the mosquitoes only by the wire screen partition, were not affected. In this camp ten cases[23] of yellow fever in all were produced by the bites of mosquitoes; no other cases occurred than those that were inoculated for the purpose, and in every instance the period of incubation was within six days. One case was produced by the bites of three insects thirty-nine days after they had fed upon a yellow fever patient; two of these insects applied to a non-immune fifty-one days after contamination brought about an attack of yellow fever, and again infected another individual fifty-seven days after they had fed upon the patient. It appears from this that contaminated mosquitoes may retain the power to infect as long as they live.

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[23] Reed, Carroll, and Agramonte. The Ætiology of Yellow Fever, an Additional Note. *Journal of the American Medical Association,* February 16, 1901; and Experimental Yellow Fever. *American Medicine,* July 6, 1901.

It was also demonstrated in four cases that yellow fever could be conveyed by means of the subcutaneous injection of 2.00 c. c., 1.5 c. c., 1.00 c. c., and 0.5 c. c. of blood drawn directly from the venous circulation of a patient in the first and second days of the disease.

At the same time another series of experiments was undertaken, which show that yellow fever cannot result from exposures to fomites. A tightly sealed building, completely protected by wire screen doors and windows, heated to summer temperature, kept dark and provided with moisture, was stocked with a large supply of articles of bedding and clothing that had been used for cases of yellow fever, some of which were fatal. The articles were purposely soiled with black vomit and the discharges from a number of patients., Three non-immunes then slept in this room for twenty nights. Each night before retiring they unpacked these soiled articles from boxes, handled and shook them, and then hung them up on nails about the room. Every morning upon rising, they removed the blankets, sheets, etc., from the walls, handled them as before, and then repacked them in the boxes, where they remained until the following night. Additional supplies of recently soiled articles were added from time to time as rapidly as they could be procured, and the procedure was then repeated by two other non-immunes for three weeks. These were in turn succeeded by two more for a similar period, and notwithstanding that some of these men slept in the garments and bedding in which yellow fever patients had died, while others slept with their faces in contact with blood drawn from yellow fever patients in the early stage of the disease, none of them contracted yellow fever. Four of these men were shown by subsequent inoculation to be susceptible to the disease. Upon these experiments we based our conclusion that yellow fever could not be contracted by exposure to fomites, and upon them were also based the measures subsequently instituted by Dr. Gorgas, the result of which has been the complete eradication of yellow fever from Havana for over three years. Cases are frequently imported there from Mexico, but by carefully guarding the patients against mosquitoes any extension is easily prevented and they are handled without fear.

In the spring of 1901, Dr. John Guiteras, of Havana, infected a non-immune by the application of an insect from our stock. In August of the same year, he succeeded in infecting seven additional subjects by means of the mosquito, and three of these persons died.[24] One of the fatal cases was an American woman, a nurse employed at Las Animas Hospital, who offered herself for the experiment. The high rate of mortality in these cases removed all doubt as to the virulent nature of the attack induced by the bite of the mosquito, and the autopsy upon the first fatal case, which it was my privilege to perform, established the presence of the characteristic lesions.

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[24] *American Medicine,* November 23, 1901, p. 811.

In the summer of that year (1901), Dr. William H. Welch, of the Johns Hopkins University, called the attention of Dr. Reed[25] to the experiments of Loeffler and Frosch, in which they had shown that the specific infectious agent of foot and mouth disease in cattle would pass through a porcelain filter and was therefore too small to be discovered with our microscopes.

The occurrence of an outbreak of yellow fever, in 1901, in Santiago de las Vegas, near Havana, offered an opportunity to obtain cases for the purpose of testing whether the organism of yellow fever could also be passed through a standard bacteria-proof filter, and it was decided, upon my suggestion, to test at the same time the effect of moderate temperature upon the infectious property of the serum.

I reached Havana on August 11th, and was quartered at Las Animas Hospital, which was provided with a good laboratory, and where inoculation experiments were being conducted by Dr. Guiteras. On the day of my arrival Dr. Guiteras's first patient was taken sick, and with his consent, I prepared to draw blood on the following morning. When the time arrived Dr. Guiteras and the director of the hospital, Dr. John Ross, decided against the procedure, and I was not permitted to use any of the seven cases that occurred within a few days. This was a great disappointment, because my time was limited for official reasons and cases had become very scarce in Havana in consequence of the measures that had been instituted against the mosquito. The excitement following the fatalities that occurred later among Dr. Guiteras's cases rendered it exceedingly difficult for me to procure willing subjects. Permission to apply mosquitoes to the last six subjects had also been refused, but through the courtesy of the chief surgeon, Colonel Valery Havard, I was permitted to use some of Dr. Guiteras's infected insects. I had been told by Dr. Guiteras and Dr. Ross that further inoculations with the mosquito were not justifiable, and should not be made, but as it was practically impossible to obtain a suitable case otherwise, I determined to proceed. I was firmly convinced, and I am still, that in healthy subjects inoculated with yellow fever, judicious treatment will insure a lower death rate than obtains with typhoid fever. Fortunately, all our purposely inoculated patients recovered.

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[25] Reed and Carroll, The Ætiology of Yellow Fever, a Supplemental note. *American Medicine,* February 22, 1902.

On September 16th, with his free consent, I applied four mosquitoes to a Spanish immigrant. One of these insects had bitten the subject of a fatal case fifty-three days previously, and the other three had also bitten the subject of a fatal case thirty-four days before. This man's attack was severe, but he made a perfect recovery. I drew blood on the second day, but an accident, caused by a careless assistant, compelled me to abandon the experiment. I was prepared to draw blood again on the third day, but the patient protested and I did not wish to alarm him.

My second case occurred October 13th, in another Spaniard to whom I had applied, four days previously, eight mosquitoes, eighteen days after they had bitten the last patient. Blood was drawn from him on the second day, the serum separated, diluted with an equal quantity of sterilized water, and passed through a new, sterile Berkefeld filter. Three c. c. of the filtrate were injected into each of three non-immunes on the following day, with the result that, in a little over four days, two of them were attacked with yellow fever. The integrity of the filter was tested and found to be perfect. The test was made by passing through it a bouillon culture of *Staphylococcus aureus.*

Another set of experiments had been undertaken with the clot that remained after the serum had been drawn off. A little sterile water was added and the whole whipped up in a sterile mortar with a sterilized egg-beater. A double water bath had been arranged and kept at a temperature of 55° C. A portion of the fluid blood mixture in a test tube was then immersed in the bath, and shaken several times until it became warm; the immersion was then continued for ten minutes longer, after which the tube was removed and plunged into cold water. Three recently arrived Spanish immigrants were each given 1.5 c. c. of this heated mixture subcutaneously, and another received 0.75 c. c. of the portion that had not been heated. The man who received the unheated blood mixture was attacked with yellow fever five days and two hours later; the three who had received the same material in double the quantity, after being heated, remained in perfect health.

You will recall that only two of the three persons who received the injection of filtered serum were infected. The third was perfectly well on the seventh day, shortly after the expiration of which he was given a subcutaneous injection of 1.5 c. c. of blood drawn directly from one of the positive cases produced by the serum filtrate that had failed to infect him. The blood that he now received was drawn early in the fourth day of the attack. Just twenty-four hours later he was taken ill with a mild but typical attack of yellow fever. Much as I desired to pursue the work further, my limited time had almost expired, and I was under the necessity of returning to the United States.

Since we began our work in 1897, we have obtained the following original results:

1. *Bacillus icteroides,* Sanarelli, and the hog cholera bacillus are practically identical.
2. Yellow fever is transmitted by the mosquito *Stegomyia fasciata.*
3. This mosquito may convey the disease as early as on the twelfth day after biting the patient, and it may retain the power to do so as long as it lives.
4. Yellow fever can be transmitted by the hypodermic injection of blood drawn from a patient in the first, second, or fourth days of the disease.
5. Yellow fever is not communicated by fomites.
6. The infectious agent of yellow fever can be

passed through a filter that is impermeable to ordinary bacteria.

7. The infectious property of blood drawn from yellow fever patients is destroyed by a temperature of 55° C., maintained for ten minutes.

Our demonstration of the power of the mosquito to convey the disease has been confirmed by Guiteras,[26] in Havana; Parker, Beyer, and Pothier,[27] in Vera Cruz; Marchoux, Salimbeni, and Simond,[28] in Brazil; and Ribas and Lutz,[29] in San Paulo, Brazil. The French commission confirms the statement that the infectious agent passes through the Berkefeld filter, and reports also that it passes through the Chamberland bougie F, but is retained by the bougie B. They found that in defibrinated blood, kept under vaseline oil, the virus was still active after five days, but inactive at the end of eight days; that the virus was rendered inert by exposure to a temperature of 55° C. for five minutes; that a relative immunity could be conferred by the injection of *(a)* the serum heated at 55° C. for five minutes; *(b)* defibrinated blood kept under vaseline oil at the laboratory temperature for eight days; that the serum of convalescents possessed both preventive and therapeutic properties; that a mosquito could become infected only by biting a patient in the first three days of the disease; that it was not dangerous until after the lapse of at least twelve days thereafter; that the bite of the infected mosquito did not necessarily produce yellow fever (in a susceptible person); that the bite of an infected mosquito, when without effect, did not confer immunity; that the disease was not produced by contact with the patient, his excreta, or personal effects; that the only known means of infection was the bite of *Stegomyia* or blood injection; that yellow fever could be contracted only where *Stegomyia* was present; that the prophylaxis of yellow fever rested entirely on measures directed against the mosquito; that the period of incubation could be prolonged to thirteen days; and that they had not been able to find the specific agent of the disease. They also record the fact that 0.1 c. c. of virulent serum injected under the skin is sufficient to produce an attack of yellow fever.

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[26] *American Medicine,* November 23, 1901, p. 811.

[27] *Bulletin No. 13,* Yellow Fever Institute of the Public Health and Marine Hospital Service, Washington, 1903.

[28] *Annales de l'Institut Pasteur,* Tome xvii, No. 11, November, 1903.

[29] *Revista Medica de Sao Paulo,* Tomo vi, No. 4, February 28, 1903.

The case in which a period of incubation of twelve days and two hours was observed, was a man to whom had been given 5. c. c. of heated serum twelve days previously and again seven days before inoculation another injection of 10. c. c. of heated serum. His remarkably mild attack followed the injection of 1. c. c. of blood drawn from a severe case in the third day of illness. This gives a probable significance to the case reported by Parker, Beyer, and Pothier[30] in which a mild attack followed the subcutaneous injection of 0.033 c. c. of filtered serum after an incubation period of nine days and twelve hours. It also directs attention to the case reported by us[31] in which a mild attack followed twenty-four hours after the injection of 1.5 c. c. of blood drawn early in the fourth day of the disease. The subject of this experiment had been given 1.5 c. c. of the filtered serum seven full days before, without result. He reported some vague symptoms on the fourth day, but his temperature did not rise above 99.4° F.; after the expiration of the seventh day he was interrogated and said that he "had never felt better in his life," and his bright, active appearance fully sustained the assertion. It seems probable that the serum injection that did not produce an attack may have exerted some influence in shortening the period of incubation after the injection of blood seven days later.

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[30] *Bulletin No. 13*, Yellow Fever Institute, 1903, p. 36.

Sternberg[32] states that, in 1887, Dr. Ruis, of Vera Cruz, injected a hypodermic syringe full of blood drawn from a patient in the eighth day of the disease into a non-acclimated individual. The result was negative.

In conclusion, I desire to invite your attention to some determined attempts at self inoculation with black vomit, blood serum, etc., from yellow fever patients, that were made one hundred years ago, by a student of the University of Pennsylvania, named Stubbins Ffirth, who embodied a description of them in a graduation thesis[33] presented to the provost, trustees, and professors of the university, on June 6, 1804. During the yellow fever epidemics of 1802 and 1803, in this city, he made numerous attempts to inoculate himself by depositing fresh black vomit and blood serum obtained from patients in the early stage of the disease, into incisions made in his arms and legs. Besides numerous other experiments he inserted four drops of such serum into an incision in his leg. One must read this interesting treatise in order to appreciate fully the determination of the investigator who administered black vomit to animals, injected it into their circulation, and deposited it in his own tissues. He inhaled the fumes from six ounces of this material, which he heated over a sand-bath in a small room; the residue was then made into pills and swallowed. Failing in this, he further tried to inoculate himself with blood serum, saliva, perspiration, bile, and urine, and finally concluded that yellow fever was neither infectious nor contagious. Since the French commission has told us that 0.1 c. c. of virulent serum is sufficient to infect, we can safely say that Stubbins Ffirth came very near to proving the inoculability of yellow fever more than a century ago.

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[31] Reed and Carroll, The Ætiology of Yellow Fever, a Supplemental Note. *American Medicine,* February 22, 1902, Cases IX and X.

[32] Buck's *Reference Handbook of the Medical Sciences.* New York, 1889, Vol. viii, p. 48.

[33] *A Treatise on Malignant Fever, with an Attempt to Prove its Non-Contagious Nature.* By Stubbins Ffirth, House Surgeon of the Philadelphia Dispensary. Printed for the Author by B. Graves, No. 40 North Fourth street, Philadelphia, 1804.

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THE LEISHMAN-DONOVAN BLOOD PARASITES (A SYNOPSIS).*

BY

JOSEPH McFARLAND, M.D.,

of Philadelphia.

The specimens that I have the pleasure of presenting to the society this evening were sent to me by Dr. Low, of the London School of Tropical Medicine, at the request of Sir Patrick Manson, to whom I had previously written, stating that our hematologists, having no opportunity to see them, were nevertheless much interested in the Leishman-Donovan blood parasites. Assuming that the honorary members of our society would be sufficiently interested in its work to make occasional contributions to its meetings, I begged Sir Patrick Manson, should it put him to no personal inconvenience, to send us some stained specimens showing the parasites, and I am glad to say that my request met prompt and generous response.

In order that the best possible use may be made of the specimens, I have thought it appropriate to synoptize briefly what is known about the interesting objects, in order that their examination may be profitable to all.

They seem to have been first described by Major W. B. Leishman,[1] professor of pathology in the Royal Army Medical College, London, in a paper entitled, "On the Possibility of the Occurrence of Trypanosomiasis in India." The parasites were first observed in cases of what Leishman called "dumdum fever."

Dumdum is a station about seven miles from Calcutta, and is notoriously unhealthy, malarial fevers of all types, dysentery, and enteric fever being rife. It is excessively damp, and, in the rains, is practically a morass from the fact of its lying so low; it is said to be even a few feet below the level of the Hoogley, which flows within a mile or two of the cantonments.

Leishman had a short personal acquaintance with this station in 1890, and the memoranda contained in his first paper, refer to the features of this form of Indian fever as represented by soldiers invalided on account of it from

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* Paper read before the American Society of Tropical Medicine, at its meeting on March 21, 1904.

Dumdum to the Royal Victoria Hospital, Netley, during the past three or four years.

> "The cases were, as a rule, regarded as having been malarial in origin, and on admission to Netley, the patients presented an extreme degree of cachexia; it was, in fact, the severity of this cachectic condition and the frequency of its association with Dumdum—and, more rarely, its immediate neighbors, Calcutta and Barrackpore—which gave rise to the idea that we were dealing with a specific type of fever, whose cause was unknown. Clinically, these cases presented no very definite features distinguishing them from other and commoner forms of tropical cachexia, the chief symptoms being an irregularly remittent type of fever, grave anemia, progressive muscular atrophy, and great enlargement of the spleen. Digestive and bowel derangements were frequent, the latter often a legacy of previous dysentery. In none of these Netley cases were malaria parasites found in the blood, nor were there any records of their having been found at an earlier stage of the disease. The difference then between these cases of dumdum fever and other cases of tropical cachexia, associated with a low form of fever, was chiefly one of degree, and this was so marked that one of the first questions one asked a patient suffering from a particularly severe form of cachexia was as to whether he had served recently at Dumdum."

On making smear preparations from the spleen pulp, in one of his cases of dumdum fever, Leishman was struck by the curious appearance among the spleen cells and red corpuscles

> "of enormous numbers of small round or oval bodies, two or three microns in diameter, which corresponded to nothing I had previously met or had seen figured or described. They stained faintly with methylene-blue and with hematin, showing with these stains a sharply contoured circular or oval shape, but no detailed structure; but on staining them by Romanowsky's method, they were found to possess a quantity of chromatin, of a very definite and regular shape, which clearly differentiated them from blood-plates or possible nuclear detritus. This chromatin appeared in the form of a more or less definitely circular mass or ring, applied to which, though apparently not in direct connection with it, was a much smaller chromatin mass, usually in the form of a short rod set perpendicularly or at a tangent to the circumference of the larger mass. The outlines of the sphere or oval enclosing these masses of chromatin were only faintly visible by this method of staining. These little bodies were scattered freely among the cells, as a rule isolated one from the other, but here and there aggregated into clumps composed of 20 to 50 members."

The bodies were not present in all cases, as Leishman mentions two fatal cases of dumdum fever in which he was unable to find anything of the same nature in the spleen. The original article continues with a speculation as to the nature of the parasites, in which Leishman unfortunately falls into error, and supposes the bodies to be degenerating trypanosomes.

On July 11, 1903, the *British Medical Journal* published a letter from Captain C. Donovan, Second Physician, Government General Hospital, Madras, regarding the bodies just described. In this letter he says:

> I wish to state briefly that I have noted bodies similar to those described by him (Leishman) in smears taken postmortem from enlarged spleens of patients—natives of India—said to have died of chronic malaria. I obtained them in three consecutive cases on April 9, 23, and 24, 1903. In the first instance, I thought I had discovered the long sought for resting-stage form of the malarial parasite in man, but could not compare them with any analogous stages in the sporozoa. However, on again procuring the same bodies in the two other cases, I changed my views, and considered they were probably postmortem degenerations of the nuclei of the splenic pulp cells. On reading Major Leishman's paper, I at once recognized the similarity of his socalled degenerations of the trypanosomes to those found by me in the spleens of the cadavers mentioned. Yesterday (June 17) I had occasion to puncture *intra vitam* the spleen of a native boy, aged 12, suffering from irregular pyrexia, with no malarial parasite in his peripheral blood (careful examination of stained films on four several occasions), and found identical bodies in the blood from the spleen, thus removing any doubt there was as to the products being due to postmortem changes. It is unwise to theorize on the insufficient grounds at present in hand. I hope to contribute something more definite on the subject after further and more prolonged study of these organisms. My films were stained by the Maurer-Romanowsky method. I am familiar with the appearance of trypanosomes—*T. evansi*, *T. lewisi*, and a doubtful species occurring in the blood of the common Indian squirrel (*Scirrus palmarum*). There was nothing resembling trypanosomes in the peripheral blood of the boy in question.

Major Ronald Ross,[2] professor of tropical medicine, University of Liverpool, published a paper entitled, "Note on the Bodies Recently Described by Leishman and Donovan." Having obtained some stained specimens of the bodies from Captain Donovan, Major Ross examined them with great care and publishes the following brief notes in verification of the previous papers:

> All these preparations contain bodies agreeing exactly with Leishman's description, and he himself admits the similarity after having been so kind as to examine the specimens.
>
> In Donovan's specimen of April 9 (postmortem) the bodies number about 30 in a field and measure about 2.5 microns. They are disconnected from each other, but often lie fairly close together in groups of 10 or more. In the specimen of June 17 (*intra vitam*) they number only about 1 in 12, they are in fields, but are slightly larger—up to 3.25 microns. In that of July 4 they are also large, and number about one in every field or so; while groups of from 2 to 12 of them can often be found embedded in what seems to be some kind of matrix which stains a faint bluish-gray color, and which has an oval contour measuring up to 8 microns in the long diameter. Some of the bodies

appear even to be intracorpuscular, but this may be due to accidental superposition.

Both large and small nuclear masses are almost invariably present, and both are always stained a deep vivid crimson. The smaller one is very often rod-like and pointed at the large one, just as Leishman describes, and stains somewhat deeper than it. The bioplasm is generally colorless, but its contour is reddish in the specimens made *intra vitam.*

In none of the specimens can I find either entire trypanosomes or the remains of dead ones, such as the characteristic flagella.

Major Ross finds it difficult to adopt Leishman's view that the bodies are involution stages of trypanosomes in the postmortem spleen, believing that the stained flagella are always to be seen in degenerating trypanosomes yet are never to be seen in the Leishman's bodies.

If, then, these bodies are nothing but disintegrating trypanosomes, we should certainly find a few of the flagella among them. Then, again, neither the large nor the small nucleus in the preparations seems to me to recall those of trypanosomes; and they are, moreover, approximated in a much more regular manner than, I think, we observe in dead trypanosomes.

Lastly, as Donovan observes, his two preparations made *intra vitam* exclude postmortem changes altogether, and should, therefore, contain some unaltered trypanosomes. *Prima facie*, then, I am strongly inclined to think that we have to do with some quite novel organism. As it has already been found in eight cases of fever and cachexia, it promises to be a common and important one.

The next note seems to have been published by Laveran,[3] to whom Captain Donovan also sent specimens. He admits that the bodies are parasites, but does not regard them as either trypanosomes or hematozoa, but belives that they belong in the genus to which he has given the name *Piroplasma*, and which includes such parasites as *Pirosoma bigeminum*, which causes Texas fever in cattle, and the recently discovered *Piroplasma hominis*, causing the tick fever of the Bitter Root Valley.

According to Laveran the bodies are found contained in the red corpuscles, and are sometimes pyriform. No one else seems to have observed the parasites in the corpuscles.

Major Ross[4] published a paper entitled "Further Notes on Leishman's Bodies." In this contribution Ross calls attention to the very important fact that in preparations of the Leishman's bodies made *intra vitam*, the organisms appear under two distinct conditions, *viz.*, free, and embedded, to the number of one up to twelve in a matrix. In the majority the contour is elliptic, but it is occasionally nearly circular. The two chromatin masses are generally situated at the extremities of the minor diameter of the elliptic cell. The larger mass often seems to bulge beyond the cell wall. He thinks that both masses are always present, but that the smaller one may be occasionally hidden by the larger. All of the free forms seem to have a most definite size and structure. The bodies embedded in a matrix are found only in preparations made *intra vitam.* They are much less numerous than the free forms. However, the contour of the little cell is generally much less distinct in the embedded organisms than in the free ones, although the chromatin is stained just as deeply and the two chromatin masses bear just the same relations to each other as regards position and distance. What he calls the matrix is always stained very faintly in these specimens, much more faintly than the red or white corpuscles. In Romanowsky specimens, the tint is violet, or more rarely mauve. The structure appears cloudy, or perhaps granular, or even stromatic; but is too delicate for expression in the drawings. The form is generally a more or less regular oval, but sometimes the mass appears to be shapeless or torn. The outline is sharp, but it is important to note that there is never any contour line suggestive of a cell wall, as with the Leishman bodies themselves. Also there is never any suggestion of the hemoglobin of the red corpuscles, or the nucleus of the white corpuscles, to be seen in this matrix. The size varies in my specimens from about three microns to eight microns in the long diameter, and there is a rough but only a rough correspondence between the size of the matrix and the number of Leishman bodies it contains. Sometimes a considerable part of the matrix is empty, and sometimes a rather large matrix holds only one of the bodies. It may contain as many as twelve.

In discussing the nature of the bodies, Ross says that after having examined some thousands of them, he has seen only two or three lying in contact with red blood-corpuscles, and therefore believes the cases mentioned by Laveran, in which they were found in the red blood-corpuscles, to have depended upon accidental superposition. He did not find any distinctly pyriform bodies in his preparations. The matrix of the embedded forms does not present any of the characteristics of a red blood-corpuscle altered by parasitic infection.

Instead of accepting Laveran's classification of the organism among the piroplasmas and accepting the name given—*Piroplasma donovani*—Ross believes the parasite belongs to another new genus, for which he suggests the name Leishmania. Should this name be accepted, the full name of the parasite would be *Leishmania donovani* (Laveran).

In the same number of the same journal, we find an additional note by Donovan, stating that up to November 5, 1903, he had found these parasites in 16 cases, in all of which they were obtained by punctures in the spleen and liver during life.

Briefly synoptized, the symptoms with which the parasites were associated were enlarged spleen and liver, irregular pyrexia, paroxysmal edema of the feet, congestion of the lungs, occasional subcutaneous hemorrhages, and cancrum oris. Medication by quinin, arsenic and sodium salicylate proved ineffectual.

The most recent contribution appears in the *British Medical Journal* for January 23, 1904, under the title "The Leishman-Donovan Body and Tropical Splenomegaly," by Sir Patrick Manson and George C. Low, of the London School of Tropical Medicine. In this paper the writers notice that over and above the malarial cases and those of leukocythemia, cirrhosis of the liver and other well-recognized pathologic conditions associated with enlargement of the spleen, there is a considerable residuum of cases of tropical disease in which enlargement of the spleen is a prominent feature, and which hitherto have not been adequately recognized or explained.

Clinically these cases fall into two categories, the subacute and the chronic. In the more acute forms there is a history at first of a malaria-like condition with recurring attacks of high fever, which after some months, and in spite of liberal dosing with quinin, leads to the development of a very definite cachexia. This cachexia is characterized by quotidian fever, afternoon chill, followed by high temperature and profuse sweating, and terminating by the following morning in a subnormal temperature and anemia. Although in some instances there may be intervals of apyrexia of several weeks' duration, in others there is little variation in the quotidian recurrence of fever, which is absolutely uninfluenced by quinin. In time the spleen enlarges, and the anemia becomes intense. According to their experience, the patients die in a few months. The fatal event is brought about sometimes by pure asthenia, sometimes by cerebral thrombosis, sometimes by diarrhea, sometimes by other intercurrent disease.

The second type of febrile splenic enlargement to which they refer, resembles the foregoing, only the fever is much milder, rarely exceeding 101° F., the splenic tumor and the anemia being less pronounced. There is, however, always a malaria-like initial stage, and just as in the other type, this and the subsequent course of the disease are unaffected by quinin. What the ultimate fate of these more chronic cases may be, is not known, but it seems probable that these patients drift along as valetudinarians until they are ultimately cut off by some other affection, to which their persistently enfeebled state renders them specially liable.

In both types of the disease the tongue is clean, the appetite good, and, but for weakness, the patient feels fairly well. Occasionally, as might be expected, in persons coming from malarial localities, attacks of genuine malarial fever may be interpolated. In this event there may be considerable gastric derangement, and quinin may be of temporary service.

In certain instances the skin becomes deeply and fairly uniformly pigmented. Owing to this latter circumstance, and because most of the cases which have passed under the observation of Manson and Low, have come from Assam and the Indian Terai, they have arrived at the conclusion that the disease is none other than what is known by the natives in Assam and India as kala-azar or kala-dunkh. They have seen an exactly similar condition in a patient from South Africa, but whether his case and the Indian disease are identical, they are not prepared to say.

Manson and Low were fortunate enough to be consulted by a patient from the neighborhood of Darjeeling, who was persuaded to enter the tropical wards of the Seamen's Hospital. From the enlarged spleen of this patient two tappings were made. In the material thus secured, microscopic examination revealed a great number of the Leishman-Donovan bodies, many fields of the microscope showing dozens of them.

Their studies of the bodies confirm and supplement the descriptions of the earlier observers, and seem to disprove completely Laveran's statement that the bodies are parasites of the red blood-corpuscles, and a species of piroplasma; although the parasites were frequently encountered superposed on or underlying a red blood-corpuscle, nothing was at any time seen to suggest that they were inside the corpuscle. The Romanowsky stain gave by far the best results. Fuchsin was a complete failure. The somewhat lengthy description of the different appearances presented by the parasite adds very little to what had already been described. Different-sized, oat-shaped, elongate and spheric bodies with a nucleus and centrosome (?), arranged as described by Leishman, similar bodies enclosed in rounded, zooglea-like masses, sometimes singly, sometimes in large clusters, and zooglea masses containing no parasites were found. They do not doubt that the frequency with which the body was found by Donovan and the frequent occurrence of chronic febrile splenomegaly, indicate that this parasite is important in tropical pathology.

Judging from the appearances met in our preparations, it seems fairly safe to assume that once in the spleen it multiplies by simple division. Certain of the parasites, after being liberated from the zooglea masses, are destined for passage into another phase outside the body, others for endogenous multiplication. The latter on becoming free in the splenic pulp probably conjugate, and throw out a material which ultimately forms the matrix of the zooglea masses within which the parasites divide for some five or six generations. This goes on indefinitely, apparently.

Thinking that the blood might be the medium by which the parasite travels toward its exogenous phase, we made repeated and prolonged examinations of peripheral blood obtained from the patient at regular intervals of two hours during the day and night. Although two expert assistants worked at these films for several days, no Leishman-Donovan body, with one doubtful exception, was ever found by them or by ourselves. Neither in these examinations of the peripheral blood nor in those of splenic or hepatic blood did we ever encounter malarial parasites or malarial melanin.

It is evident that the parasite must get out of the body somehow, and that the blood is the most probable channel. We thought that possibly the parasite was filtered out from the splenic blood as the latter passes through the liver in the portal circulation. Accordingly, we tapped our patient's liver, and found in the small quantity of blood so obtained, numerous single or double parasites, but no zooglea masses. This discovery seems to point to the biliary ducts as the channel through which the parasites escaped to gain subsequent freedom by passing out of the body with the feces, but repeated examinations of the feces were negative. Similarly, centrifuged urine also yielded no parasites. A curious feature about the parasites from the liver was that in quite 90% of them the nucleus was either extruded and swollen, or was in process of extrusion. Possibly this phenomenon was owing to the blood having been diluted with normal salt solution. An attempt to cultivate the parasites in blood agar failed.

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RELAPSING FEVER: ITS OCCURRENCE IN THE TROPICS AND ITS RELATION TO "TICK FEVER" IN AFRICA.*

BY

F. CREIGHTON WELLMAN, M.D.,

of Angola, West Africa.

The disease under discussion—variously spoken of as famine fever, seven-day fever, fièvre à rechute, hungerpest, *febris recurrens*, relapsing fever, and, quite recently, "tick fever"—is defined by Osler[1] in the following words: "A specific, infectious disease, caused by the spirochæte (spirillum) of Obermeier, characterized by a definite febrile paroxysm, which usually lasts six days, and is followed by a remission of about the same length of time, then by a second paroxysm, which may be repeated three, or even four times."

Since the epidemic, about 1870, in New York and Philadelphia, and the description of the parasite by Obermeier in 1873, the disease has not attracted much attention in the United States, and I bring it before the readers of this journal, not as a condition which is of great present concern to the student of the endemic affections of our own country, but as a disease of warm climates, having a wider distribution than was formerly supposed, and which may prove to be of much interest and importance to students of that branch of pathology known as "tropic medicine." Relapsing fever is not described in the usual books on tropic diseases, *e. g.*, Davidson, Manson, Scheube, Brault, Fisch, etc., but we know that it has long been common in India, and is known in China, the East Indies, and other parts of the Far East, and an examination of current medical literature reveals its existence in several quarters of Africa.

My attention was specially drawn to the existence of spirillary fever in warm countries by a typic case of the disease, which was brought to my notice some months ago in Angola, West Africa, and which I have recently published in another periodical.[2] I have accordingly

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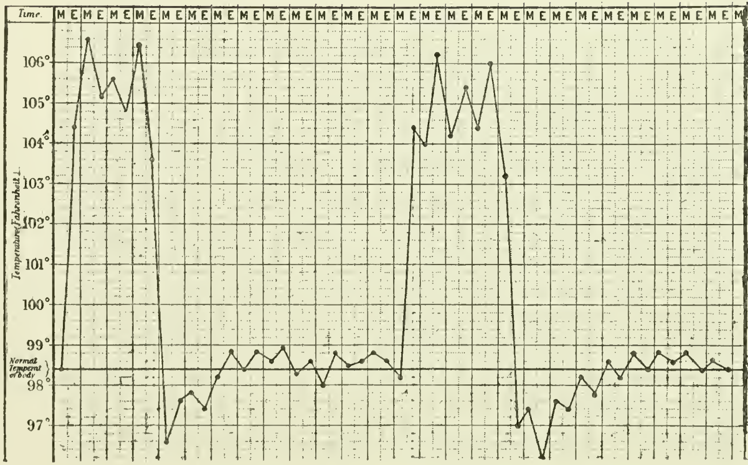

Chart I.

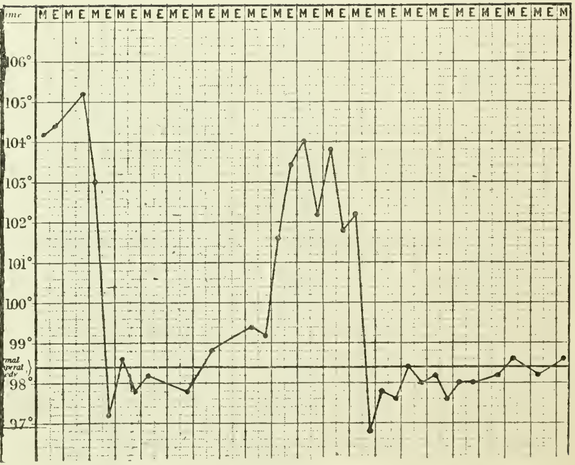

Chart II.

Chart I.—Temperature chart of case of relapsing fever occurring in the United States. Chart II.—Temperature Chart of Case I.

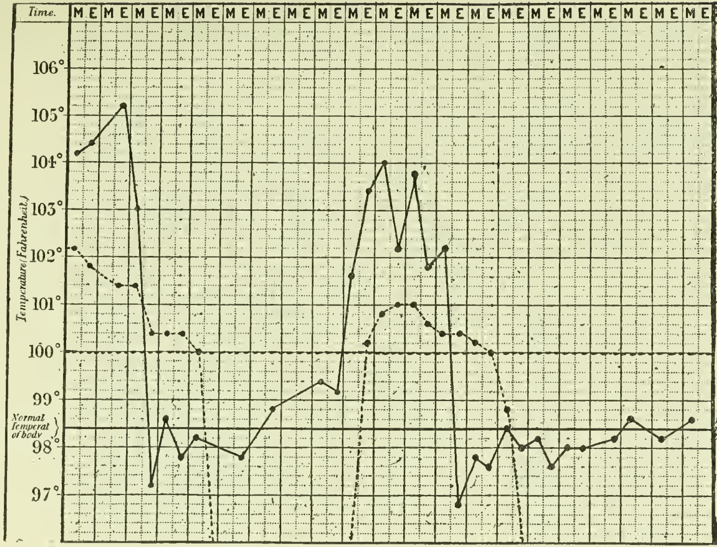

Chart III.

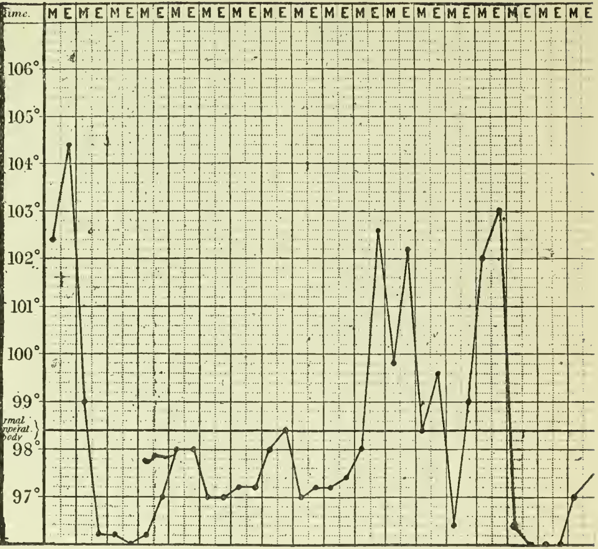

Chart IV.

Chart III.—Combined Blood and Temperature Chart of Case I. Description of Chart.—The temperature is represented in the usual manner, by an unbroken line. The dotted line represents the comparative abundance of the parasites in the blood during different stages of the attacks, taking the line marked 100° as representing the average of one parasite in each field. Thus 101° would mean 6 parasites in each field, 102° 11 parasites, etc. I have not tried to compute the number of parasites in a given volume of blood, as my object was rather a study of the relation between the temperature and the presence of parasites in the blood throughout the attacks. Chart IV.—Temperature Chart of Case II.

brought together the records of a few cases reported from the tropics, which I herewith present, together with some remarks on the parasite and its probable carriers. It will be seen by the notes and charts reproduced that the disease is, so far as can be gathered from the incomplete data available, but slightly different (possibly somewhat more atypical) from relapsing fever in cooler lands.

CASE I.—Author's case. (From Angola, West Africa.) The patient was a Bantu man, aged 32, and was first seen on March 3, 1904. He stated that he had been taken ill with fever the day before admission. He had had no rigor or vomiting. There were pains in back and limbs. He had had no previous attack. The patient was a large man, fairly well nourished. Said he was thinner than when taken ill. Temperature, 104.4° F.; pulse, 92; respirations, 29. Pupils normal, spleen slightly enlarged. *Spirillum obermeieri* very plentiful in blood, averaging about a dozen to each field ($\frac{1}{12}$ imm. lens, oc. II). The patient appeared very comfortable, and I should not have suspected so much temperature. The temperature remained fairly stationary for two days after admission, and parasites were found in the blood during this time. On the third morning the temperature was found to have fallen to subnormal, although the parasites still persisted, but in fewer numbers, in the blood until the fifth evening, after which the blood remained clear of parasites for about a week, during which time the patient felt well and the temperature rose to normal and slightly above. On March 11 he had a slight rise of temperature, with some malaise and pains in the back, and the following day it went steadily higher, and he went to bed. There was no vomiting nor purging. The parasites were first again noticed on the evening of March 12. On March 13, there were many spirilla, although fewer than in the previous attack. They grew gradually less, and finally disappeared from the blood on the evening of March 17.

The temperature (as in the first attack) fell a couple of days before the disappearance of the parasites, and remained subnormal for a few days after the crisis. The patient continued well till he left the hospital, on March 23. I have indicated in the following chart the very definite relation between the rise and fall of the temperature and the presence of the parasite in the blood.

CASE II.—Dr. L. G. Hill[3] has published a case of relapsing fever from Pak-hoi, South China. The patient was a Chinese woman, aged 65. When first seen she had fever and delirium. Many active spirilla in the blood. History: Had fever from June 24, 1903, to July 5. On July 6, 7, and 8 she had no fever. On July 9 fever reappeared, and lasted till July 13, when she was admitted to a hospital. On the evening of July 13 it stood at 104 2° F. The next morning it fell to 99° F., and the evening of the same day to 96.2° F. It remained subnormal till July 23, on the evening of which day it rose to 102.8° F. Three days later it fell again to 96.2° F., and on July 27 rose to 103° F. On the morning of July 28 it was again subnormal (96.2° F.), and continued so until she left the hospital, on July 31. The spirilla were seen in the blood in diminishing numbers for two days after the crisis, and not again till July 23, when the fever returned, on which occasion they were plentiful but not so active as during the previous attack.

Case III.—Dr. J. C. Graham[4] reports a case of spirillary disease in Sumatra. The patient was a Chinese coolie from Swatow. The man had high fever, tenderness over both hypochondriums, pains in his joints and the muscles of the leg, beside severe headache. The ocular conjunctivas and the skin generally were icteric. The blood teemed with spirilla.

Case IV.—Christy[5] has described an epidemic of relapsing fever from the Bombay Presidency, marked by jaundice, ecchymosed conjunctivas, pains in the joints, and severe fever, with more or less weekly intermissions. He only succeeded in persuading one man (who had a temperature of 103° F.) to have his blood examined. The blood proved to be full of *Spirillum obermeieri.*

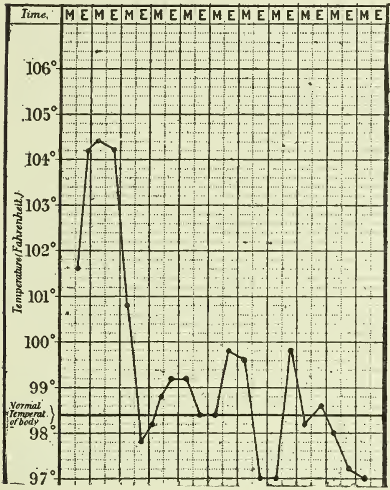

Chart V.

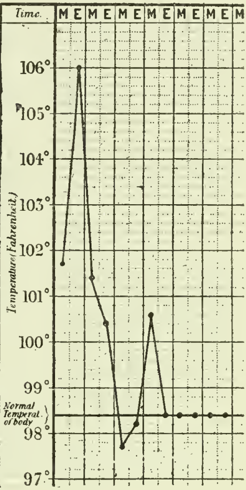

Chart VI.

Chart V.—Temperature Chart of Case VI. Chart VI.—Temperature Chart of one of Ross and Milne's cases.

The next three cases are reported by Dr. A. R. Cook[6] from Uganda, Central Africa:

Case V.—The patient was taken ill with pain in the chest and vomiting. No definite history of rigor diarrhea. Spleen and liver did not extend below ribs. Patient was in collapsed condition when seen. Temperature, 99.4° F.; pulse, 140; respirations, 80. Died three days after onset of attack. Spirilla very abundant in the blood. Autopsy showed stomach and bowels empty; liver, spleen, and kidneys somewhat enlarged. Spleen very soft. Some spirilla found in smears from liver and spleen.

CASE VI.—Temperature, 104.2° F. on admission; rose rapidly. Slight delirium. No jaundice. Chest and abdomen normal. Spirilla rather sparse in blood (one to every field with high power). Temperature fell next day to subnormal, and spirilla disappeared from blood. Patient said this was second attack.

CASE VII.—Small girl; applied for treatment for bronchitis. She had some temperature, and blood-examination showed presence of many spirilla. Temperature rose to 105° F. No jaundice. Liver and spleen could not be felt below the ribs. History of rigors, but no vomiting or diarrhea.*

The succeeding four cases are also from Uganda, and are reported by Drs. P. H. Ross and A. D. Milne.[7] The significant point about the cases is that these patients, together with four others ill with spirillum fever examined by these observers, all ascribed their illness to having been bitten by ticks. The case histories are given as follows:

CASE VIII.—Nubian private, K. A. R., stayed 14 days at Escarpment Camp Butiaba.† On his return two days later, he fell ill.

CASE IX.—Mnyoro hut tax laborer, stayed 18 days at Lake Camp, Butiaba. The day after his return, fell ill.

CASE X.—Mganda boy, belonging to Nubian soldier, stayed several days at Escarpment Camp, where he actually picked the ticks off his body each night. On the third day after his return, fell ill.

CASE XI.—Wife of Nubian sergeant, returned from Escarpment Camp, Butiaba, six days previously, and had fallen ill two days after her return.

The symptoms complained of by these tick-produced cases of spirillum fever were:

Severe pains in the head, mostly in the occipital region and back of the head; sometimes cough, pains in the back and limbs; sometimes splenic tenderness; another marked symptom was vomiting; pulse varied from 90 to 120; half of the patients had diarrhea. On examination the skin was hot and dry; there was congestion of the conjunctivas, alas of the nose dilating and contracting, tongue mottled with slight yellow fur; no enlargement of liver or spleen.

All the patients recovered. Some with spirillum fever examined by the last-named observers had a relapse, others had not. They mention one patient in whom there was no return of temperature but who, at the time when the relapse was expected, complained of severe headache and showed spirilla in his blood.

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* Dr. Cook reports an epidemic of relapsing fever in his district, of which the foregoing cases are examples.

† A station badly infested with ticks and a hotbed of "tick fever," Ross and Milne, loc cit..

Case XII.—The last case in the meager literature accessible here, likewise from Central Africa, is one reported several years ago,[8] and which was mistaken for malarial fever, but which seems to me clearly spirillary disease, and I therefore reproduce it here. The writer is speaking of the flagellated bodies of *Hæmamœba præcox* which he believed he saw and which he described as follows:

"On making a fresh specimen and examining at once the whole field seemed to be full of a mass of waving and lashing flagella coming from nearly every corpuscle. It reminded me of the rippling effect produced by the wind passing over a cornfield. . . . Careful examination in similar cases has failed to detect any 'crescent' bodies which could have been transformed into the flagellated bodies. On the other hand, the flagella generally seem to spring . . . from unaltered red blood-corpuscles."

The foregoing forms a capital description of *Spirillum obermeieri* in the blood, and there is little doubt but that this was what the writer saw. His drawings, too, are very suggestive of the parasite just named. We know that the flagellated body of malignant malaria is evolved only from the crescent or gamete, and those of us who have worked for any length of time with the disease know how very rarely the gamete is seen in the tropics. I personally saw only two crescents in a series of over 400 examinations of malarial blood. Plehn saw them but once during nearly four years' work in the Cameroons, and Ziemann, out of more than 1,000 examinations, only on 12 occasions detected isolated crescents. Then, too, the finding of "flagella" in freshly drawn blood would preclude the possibility of their being malarial microgametes. This case then, must be considered relapsing fever.

The symptoms are not indicated. The patient was an anemic and emaciated child who was very ill and died the same night the blood-examination was made.

From what has been written it will be seen that relapsing fever has a wide distribution in tropic countries. It is also quite probable that it has been overlooked in other places or mistaken for other conditions. Others may have made a mistake similar to the one I have pointed out, and, as the parasite is sometimes very scarce in the blood, it may have been overlooked in many instances. And so, while the affection also occurs in temperate climates, it would seem to have as good a claim to be ranked as a tropic disease as have malaria, leprosy, plague, and other diseases which are only partially dependent on climatic conditions for their survival. It therefore behooves practitioners in the tropics to search carefully the blood of suspected patients before making a diagnosis of "double continued fever," etc. Ross and Milne[9] write that in some of the cases in which search was made through the whole of a large blood film only two or three spirilla were found.* With these facts in mind it would seem reasonable to believe that the known distribution of relapsing fever will soon be greatly widened. The disease is now generally thought to be carried by vermin. The bedbug, *Acanthia lectularia*, and more recently the "Ocihopio" tick, genus *Ornithodorus*, of which there appear to be at least two species in Africa, have been suggested as probable hosts. The careless personal habits of savage and semicivilized peoples greatly facilitate the spread of a disease so transmitted, and its presence in most tropic countries should not therefore be a cause for surprise.

Since the publication by Marchaux and Salimbeni of their work on the spirillary disease of fowls, there has been, as I have said, a disposition on the part of some to predicate a tick as a carrier of the human spirillum also. The work of Ross and Milne, referred to, seems to establish this hypothesis. Daniels, quoted by Manson,[10] describes the violent symptoms of "tick fever" as lasting "for nearly a week. . . . After that, fever continues often for three or four weeks." Christy[11] says the natives of Central Africa "dread this tick (*Ornithodorus moubata*) and know well the symptoms occasionally following its bite. In describing these they invariably go through a pantomime indicative of vomiting, with pain in the head and abdominal region. They say that the symptoms may last for several weeks." Both these observations are certainly suggestive of the clinical course of relapsing fever. The racasu mentioned by Daniels and Christy, can be but one of several carriers of the spirillum, since spirillary disease is not confined to the hemisphere producing ticks of this species. However, Christy has seen a tick in South America which is very similar to *Ornithodorus moubata*[12] and Brault[13] mentions *Argas turicata* and *A. megnini* as being described from Mexico, *A. talaje* from Central America, and *A. chinche* from Colombia. Finally, from Persia, *A. persicus* is reported

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* Note on the parasite of relapsing fever. It has seemed to me that the socalled spirillum of Obermeier, as seen in stained specimens from the blood in my case, dies in rounder and more flowing curves than are generally described and pictured. The specimens I have measured average about 30 μ by 0.1 μ. They are sharp at the ends. The presence of the parasite in the blood had, in the case mentioned, a constant relation to the rise and fall of the temperature which I have indicated in Chart III, q.v. The spirillum, or more properly, *Spirochæta obermeieri*, is placed by many observers among the protozoa, and in view of the theories of Schaudinn (Trans. in *Jour. Trop. Med.*, June 1, 1904, et seq.) the possibility of its representing some stage in the development of a flagellate occurs to one. The development of the hemameba of a certain owl, *Athene nactua*, into a spirochæte and finally into a trypanosome as described by the author just mentioned (vid. *Archiv für Schiffs- und Tropen-Hygiene*, 1902, Vol. vi, p. 389) is particularly suggestive in this connection. In the blood of man one occasionally sees the spirilla lying together in such a fashion as to suggest the multiplication by longitudinal fission which is characteristic of other spirochætas and of trypanosomes. Tubes of hemoglobin agar, such as are prepared for the cultivation of trypanosomes, inoculated with blood from the patient whom I saw and incubated at room temperature and at 37° C. showed nothing of such multiplication and the cultures died out in a short time. I was unable to procure healthy monkeys at the time (the ones which I had were being used for the purposes of another study) so I did not try inoculation experiments with the patient's blood.

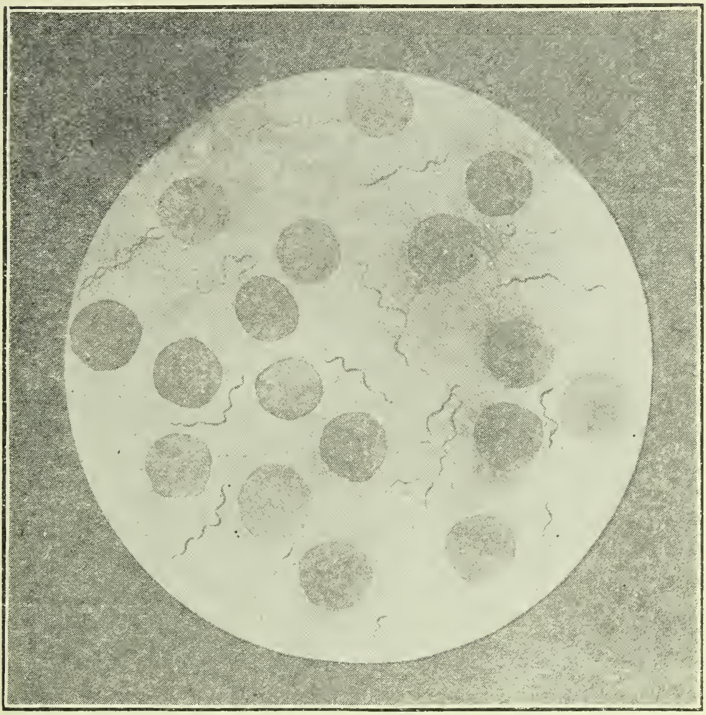

Fig. 1.—*Spirillum obermeieri.* Stained with carbol fuchsin.

as causing "tick fever."[14] Perhaps these and similar acari serve as carriers of the spirillum in other countries. Of course, the possibility of other parasites being conveyed to man by ticks must be kept in mind with the consequent possibility of there being more than one kind of "tick fever." It has been suggested by several that an African tick is one of the intermediate hosts of *Filaria perstans.*

There have been described from Africa three species of the genus *Ornithodorus*, viz.: *O. savingnyi*, Aud., *O. moubata*, Murray, which was first discovered by Welwitsch in Angola and described under the name *Argas moubata* by Murray in 1877, and Neumann has described a third variety from South Africa, *O. savingnyi* var. *caeca*, Neum. This latter is thought by some to be the same as *O. moubata*, Murray. The "Ocihopio" tick (the species of *Ornithodorus* found in this immediate locality and which I believe to be *O. moubata*, Murray) is very plentiful here. I have found as many as 100 in an hour in an old native hut. There are also at least three other kinds of ticks here. The "Ocihopio" is of a yellowish-brown color (somewhat lighter at the edges than in the middle) when small, and greenish-brown when older. The shell which is cast when the tick moults is of a pale yellow color. The chitinous covering has a rough appearance, due to its being covered with fine points all over its surface. The adults measure about 8 mm. or 9 mm. long by 6 mm. or 7 mm. broad and are deeply furrowed on both the dorsal and ventral surfaces. In the younger ones the furrows are much less marked on the ventral surface. The body is thick and rounded at the edges. There are no eyes. The feces of the tick are white. Compared with other acari the "Ocihopio" is fairly active. When placed on its back on a smooth surface which affords no hold for its legs, such as a piece of glass, it has a curious way of changing the shape of its body to enable it to roll over. The ticks hide by day in holes and cracks in the floors and walls of native huts, or in the grass thatch of old camps, and come out by night to bite. They bite man and all the domestic animals, viz., pigs, sheep, goats, dogs, etc. They are very tough, and difficult to kill.

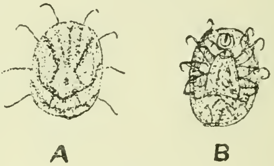

Fig. 2.

An interesting fact in connection with these ticks is that they are sometimes attacked by a fungus, which destroys them. The disease generally begins at one edge of the tick, and appears in the form of a light, almost white spot which spreads. The infected ticks are more sluggish than healthy ones.

I have not discussed in this paper the views of Nuttall, Christy, and others, on the bedbug as a possible carrier of relapsing fever, my special object being rather to point out the probable wide distribution of the disease in the tropics, and to call attention to some of the reasons for connecting it with "tick fever" in Africa. In conclusion, I would say that the preceding suggestions from an isolated tropic worker are only offered in the hope that they may elicit an adequate discussion of this interesting subject from some one at home who, with access to the necessary literature, can go much more fully into the question than is possible with one situated like I am.

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[7] British Medical Journal, November 26, 1904, p. 1453.
[8] Journal of Tropical Medicine, February 15, 1902, p. 53.
[9] Loc. cit.
[10] Tropical Diseases, p. 714.
[11] British Medical Journal, September 19, 1903, p. 652.
[12] British Medical Journal, September 19, 1903, p. 653.
[13] Maladies des Pays Chauds et Tropicaux, p. 292, seq.
[14] Manson: Tropical Diseases, p. 712.

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NOTES ON THE TROPICAL DISEASES OF THE ANGOLA HIGHLANDS.*

By F. CREIGHTON WELLMAN, M. D.,

BENGUELLA, WEST AFRICA,

MEDICAL OFFICER.

This report is a *précis* of my observations on the pathological conditions occurring in the highlands of West Central Africa, extending over eight years. In writing I have not followed any scientific classification of the diseases studied but have, for the sake of convenience, used a somewhat arbitrary division based partly upon the diagnostic procedures usually employed by the tropical practitioner. The method adopted is to mention the various diseases encountered, with their native names when such can be obtained, and generally to make only such remarks as seem called for by their local peculiarities as to frequency, severity, symptoms, etc. These notes, therefore, are not in any sense offered as a contribution to the general study of tropical diseases, which is at present engaging the attention of many distinguished observers, but rather as data deriving their main value from the fact that they were gathered in a locality hitherto unexploited by tropical pathologists. It seems that observations

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* Published under the auspices of the American Society of Tropical Medicine. I present this report through the kindness of Dr. Joseph McFarland, without whose encouragement and counsel it would not have been prepared.

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on even the more familiar tropical diseases under conditions possibly slightly different from those already understood would, if carefully made, be of some value to general students. The list will be found to consist almost entirely of tropical diseases in the usual acceptation of that term, and of those only which have been clearly recognized. Mention is made of only a few interesting cases of a doubtful nature. I have noted also the probable absence of a few diseases when I felt I had evidence for doing so. Space has forbidden the inclusion of case records and many other particulars. The attempt has been rather to prepare a digest which, while not unwieldy, will yet be of some definite epidemiological value. I have already prepared a similar report for another publication,[1] and Balfour[2] has recently done the same thing for the Sudan.

District and People Studied.—The province of Angola may be divided for scientific purposes into three regions: littoral, montane, and high tableland. The territory best known to me, and in which most of my time has been spent, lies in the last of these three divisions and is that occupied by the Bihé, Bailundo, and Andulo peoples with their allied tribes. This district lies between 13° and 14° south and consists of a plateau ranging from 5,000 to 6,000 feet above the sea level. The climate is in consequence cool as compared with other sections in the same latitude. In damp localities even slight frost is found at one season of the year. The people are Bantus, numbering about 200,000, and of a good physique. The staple article of food is maize, eaten in the form of thick, partially cooked mush with small quantities of boiled beans, cassava leaves, or meat as a relish. The dress of the people, men and women alike, is a thin skirt or cloth falling from the waist to the knee. Quite recently many of them affect a shirt in addition to this. They are porters and agriculturists by occupation and are of a contented, equable disposition. Polygamy is common. Besides this particular district I am more or less familiar with the region between it and the coast, both to the north and south of the Coanza River, especially the country lying immediately around the cities of Benguella and Loanda.

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[1] *Journal of Tropical Medicine*, London, February 15, 1904.

[2] *Ibid.*, April 15, 1904.

(1) DISEASES APPEARING FROM AN EXAMINATION OF THE BLOOD.

Malaria (native name, *Ombambi*).—The only forms of the parasite yet seen are those of the malignant type.[3] The only one of these at all common is the young ring form. I possess slides of this which show an almost incredible number of invaded corpuscles, some of which contain two and even three parasites. I have seen one very severe case which showed adult sporulating parasites in the finger blood. I believe this presence of adult malignant parasites in the peripheral circulation is a very rare condition. Of course they are very common in the brain and viscera. They are easily demonstrated (when a post mortem examination cannot be obtained) by passing a large aspirating needle through the back of the orbit into the brain or through the abdominal parietes into the spleen, giving it a circular stirring motion, then sucking up the pulp and juice thus obtained and making smears (which should be stained with Leishman's stain) and squash preparations (for pigment). This can be done without the knowledge of the natives, who hold a superstitious belief in regard to cutting a dead body. I have been puzzled over the fact that I do not see crescents in my malarial films. Of course it is quite possible that I have overlooked a few; but I have never experienced difficulty in demonstrating them in appropriate cases of subtertian malaria contracted in West Africa which I have seen in England, France, and Germany, and the crescent with its comparatively large size, definite shape, and the striking arrangement of its pigment and chromatin is not a form of the parasite easily mistaken. This brings up the query as to how the parasite is disseminated. We know that for some days after the beginning of an attack of fever the *H. prœcox,* if undisturbed by quinine, multiplies by simple schizogenesis, after which time crescents appear which we regard as young gametes and the first step in the Coccidia like stage spent in the mosquito. The extreme scarcity of crescents does not, therefore, seem to accord with the almost universal infection which obtains among residents of tropical Africa. A theory to account for this discrepancy, which I once entertained, is that in this constant temperature an earlier stage of the parasite serves as the beginning of the mosquito cycle; but as I have not seen in the peripheral blood any intermediate forms between the small intracorpuscular ring form and the gamete, I have abandoned it and now suppose that, although very rare,

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[3] It is possible that benign tertian and quartan have escaped my notice. However, it is only fair to state that I have examined the blood of many malarial patients in this district, and that the appearance of these parasites is familiar to me, they being the principal forms with which I have worked in my studies at the Seamen's Hospital of London and other places.

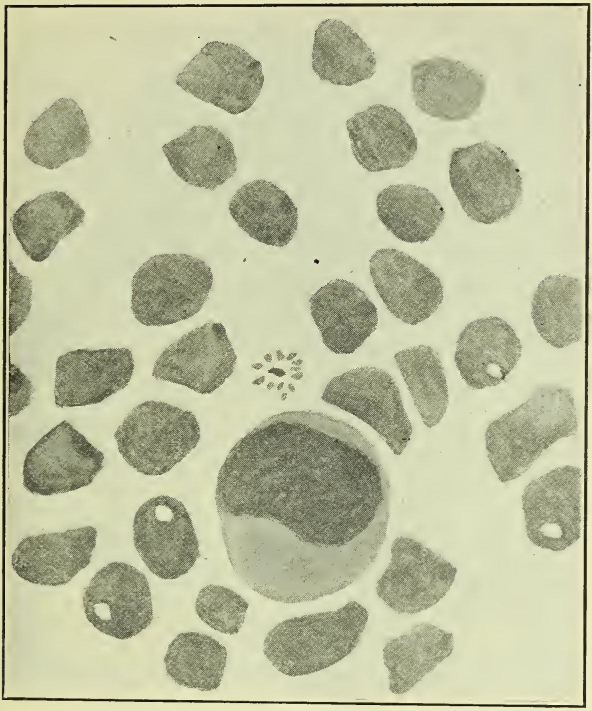

FIG. 1.—Adult sporulating malignant malarial parasite in finger blood of negro child. Young intracorpuscular ring forms are also seen. Stain hæmatoxylin and eosin.

crescents are occasionally present.[4] That they are more plentiful in temperate countries may be due to the fact that the victim's physique, in a better environment, more easily resists the intracorporeal schizogenesis of the parasite and compels it sooner to attempt sexual reproduction. This scarcity of crescents, as contrasted with their numbers when patients have relapses after reaching a temperate

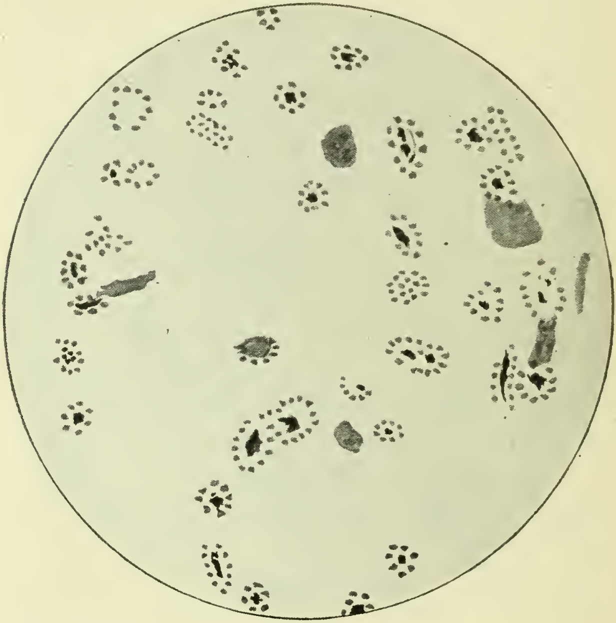

FIG. 2.—Sporulating malignant parasites from spleen puncture. Stain hæmatoxylin.

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[4] Since the above was written I have seen a blood film containing two crescents.

climate, has been remarked by other observers besides myself.

The conditions set up by the parasite are myriad. Atypical fevers are numerous and masked forms or the mimicking of other diseases, especially dysentery, are not uncommon. One peculiar form manifests itself as an obstinate low evening temperature simulating fever arising from septic process. Epileptiform convulsions are occasionally seen. The typical malignant tertian[5] fever is very frequent. Among the prodromal symptoms pain in the shins, yawning, and headache are those of which complaint is most frequently made. Rigor is generally slight, often absent. A sense of suffocation is common. Epistaxis and vomiting are occasionally seen. Temperature runs high. The spleen is almost always inflamed or at least congested, even in comparatively mild attacks. I have sometimes demonstrated albuminuria. The convulsive and comatose forms occur oftenest in children. The latter of these is frequently fatal in infants. What I take to be malarial ulcers are occasionally seen. They do not always answer to general treatment, but will nearly always heal quickly under the local application of ordinary sulphate of quinine. Cachexia is not rare. The intense anæmia set up by neglected invasions of malaria is easily detected by the physical signs. The hæmoglobin index is often higher in natives than one would judge from the patients' appearance. Microscopical examination shows poikilocytosis, a few megalocytes and microcytes, while normoblasts are quite common. A large number of apparently healthy natives have a high percentage of large mononuclear leucocytes. I have noticed the presence of myelocytes during acute attacks. The splenitis, if allowed to become chronic, sometimes results in enormous permanent enlargement. I once examined a young Portuguese lieutenant whose spleen reached to the crest of the left ilium and well to the right of the umbilicus.

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[5] While quotidian and remittent fevers are common I have not been able to distinguish between the parasites of these and the subtertian variety. I cannot see but that multiple infection accounts for such attacks.

Among the mosquitoes already familiar to zoologists which I have collected and presented to the British Museum and which Mr. Fred. V. Theobald, author of A Monograph of the Culicidæ of the World, has kindly determined for me are: *Culex creticus,* Theob.; *Culex viridis,* Theob.; *Myzomyia funesta,* Giles; *Cellia squamosa,* Theob.; *Cellia pharoensis,* Theob., and *Anopheles Wellcomei,* Theob. In addition to these I have discovered the following, which are new to science and which Mr. Theobald is describing in the *Entomologist: Culex sp. nov.* near *hirsutipalpis,* Theob.; *Culex sp. incert., Pyretophorus sp. nov.,*[6] *Genus incert.* (near *Stegomyia*) *sp. nov.*[7] The first and the last of these new varieties are remarkably common and I have bred a large number of imagoes from eggs and larvæ collected in different parts of the country. I now think that the most common anophelines are *Myzomyia funesta,* Giles, and *Cellia squamosa,*

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[6] I originally thought this was *P. costalis,* Loew. vid. *Jour. Trop. Med.* for February 15, 1904, p. 53.

[7] I do not mean to connect the culicinæ in this list with malaria, but only mention them along with the anophelinæ as being of general interest.

Theob. It is an interesting fact that in the town where the writer is stationed the number of fevers has markedly increased since the cutting of an irrigating ditch through the town a few years ago.

As regards the frequency of malarial infection I present the following spleen index of 200 untreated natives.[8]

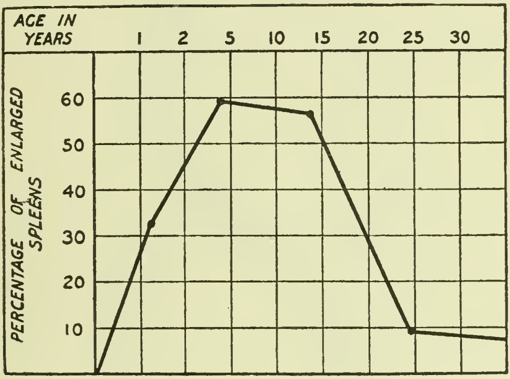

TABLE I.—SPLEEN INDEX.
(150 Children and 50 Adults.)

I believe that the best prophylaxis consists of a combination of mosquito extermination[9] and systematic administration of quinine to children. A properly made mosquito curtain is an indispensable personal precaution.

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[8] Drawn for the *Jour. Trop. Med.* (April 15, 1904, p. 124).

[9] Much has been written concerning antimalarial campaigns recently. Major Ross's work in British West Africa has attracted much attention. Good work has been also done in Africa by the French and Germans. *Vid. Archiv. f. Schiffs—u. Tropen-Hygiene,* September, 1904; *Annales de l'Inst. Pasteur,* February 25, 1904; *Archives de Méd. Nav.*, February, 1904, etc.

Filariasis.—This infection is rare. In the course of routine blood examinations of cases of suspected malaria one occasionally runs across *F. perstans.* I

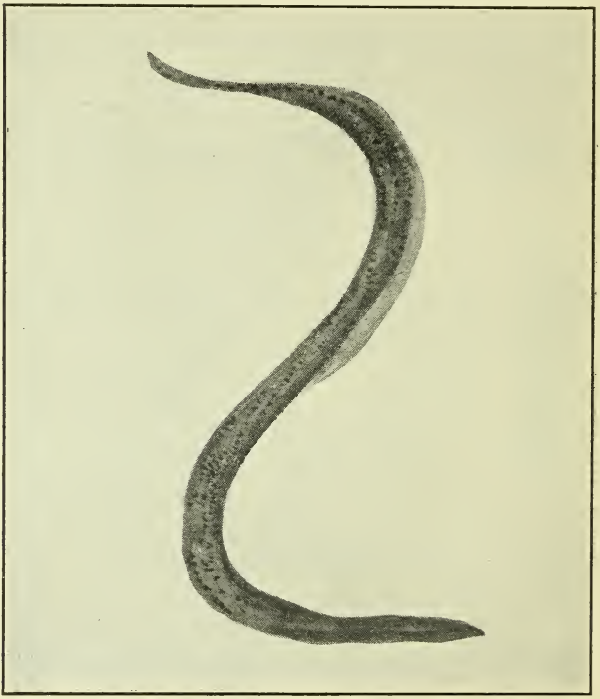

FIG. 3.—Embryo found in blood of West African negress. Stain hæmatoxylin.

also encountered in the beginning of 1904 a blood worm unknown to me. I wrote of it at that time in the following words:[10] " I found this filaria late one evening in one of about fifty blood films from as many different natives, my object being to secure *F. nocturna.* My first thought on catching sight of it under low power was that it might prove to be the *F. gigas* described by Mr. Prout.[11] But a few minutes' observation with the plate accompanying Mr. Prout's article before me negatived such a sup-

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[10] *Jour. Trop Med.,* February 15, 1904.

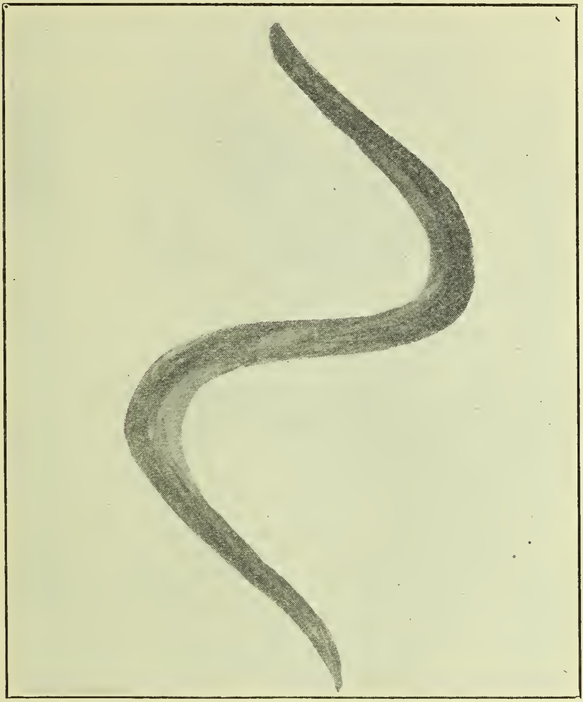

Fig. 4.—Embryo found in blood of West African negress. Stained with methylene blue.

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[11] *British Med. Jour.*, September 20, 1902.

position. Scheube[12] speaks of the occasional presence of *Anguillula stercoralis* in the blood, but on comparing stained preparations of *A. stercoralis* with the doubtful specimen it was plain that they were not the same. The new filaria stains slowly with methylene blue, but most beautifully and delicately[13] the somewhat elaborate structure showing plainly. The stained specimen exhibits very faint granules which are possibly a post mortem phenomenon. It tapers at both cephalic and caudal extremities, most markedly at the latter. Both head and tail are blunt. A line which appears to represent a central viscus extends from the head to a point near the tail." This last feature, taken together with its great thickness and general appearance, no less than the absence of V spot, tail spot,

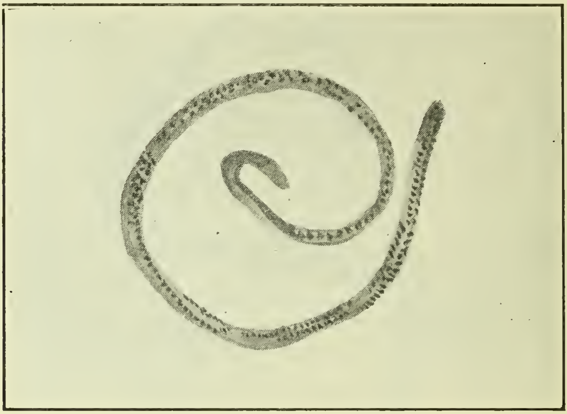

FIG. 5.—*Filaria nocturna.*

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[12] *Diseases of Warm Countries,* p. 454, note.

[13] It stains readily and deeply with hæmatoxylin.

etc., led me to doubt that it was a filarial embryo. But as it was undoubtedly a blood worm (I was using well cleaned slides and distilled water in my laboratory) I showed it to Dr. George C. Low, superintendent of the London School of Tropical Medicine, when I was in London in July, 1904. He pronounced it an entozoal embryo, which had in some unknown manner got into the blood stream. Sir Patrick Manson subsequently confirmed this

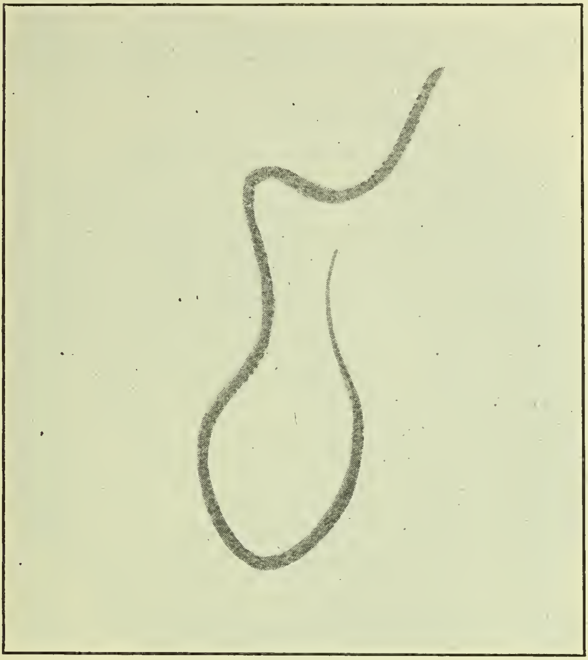

FIG. 6.—*Filaria demarquaii.*

opinion.[14] I have not yet demonstrated *F. nocturna*, although I have seen both varicose groin glands and *Elephantiasis arabum* (native name, *Ovisonyua*).

Leucocytic Variation.—This symptom may be appropriately mentioned here. Excess of large mononuclears has been spoken of under malaria. Eosinophilia seems to be sometimes present and sometimes capriciously absent in filariasis and during invasions of *Oxyuris vermicularis* and other intestinal parasites.

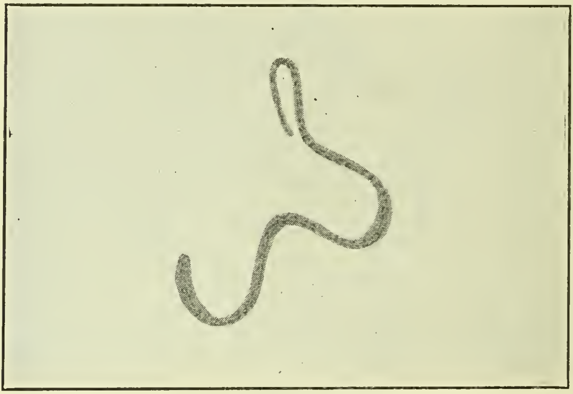

FIG. 7.—*Filaria perstans.*

Relapsing Fever.—I have recently seen a case of this affection which I hope to publish at an early date. I had not met the condition before in the course of many examinations of fresh and stained blood films, and the disease is not discussed in the standard works on tropical medicine; yet a glance at current medical literature shows that it is being recognized in many tropical countries, and that it is common in different parts of equatorial Africa. *Spirillum obermeieri* were plentiful in the blood. It seems to me that the parasite dies in somewhat larger and more flowing curves than are generally described and pictured. The convincing work of Marchoux and Salimbeni on the spirillary disease of fowls suggests that the "Tick Fever," described by Manson[15] may be relapsing fever. The spirillum

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[14] That the embryos of at least some entozoa can pierce the tissues of their host is proved by the experiments of Professor Loos with the embryos of *A. duodenale* in Egypt, some of whose preparations I have seen. Bentley's work on the ætiology of Pani-ghao in Assam proves the same thing.

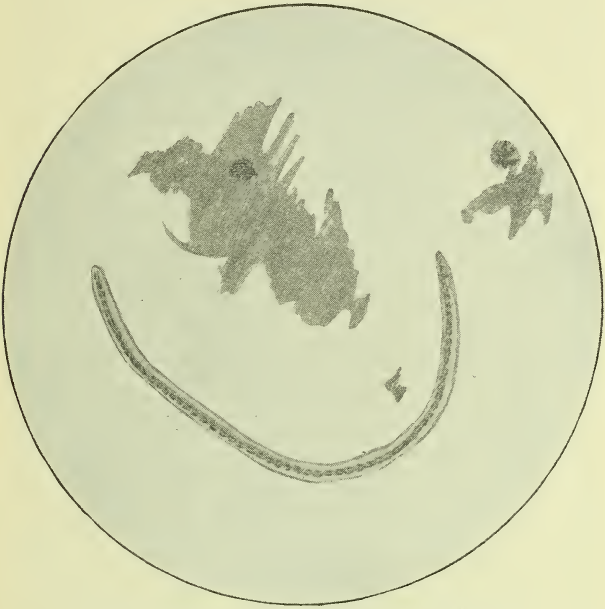

FIG. 8.—Filarial embryo seen in blood of negro.

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[15] Tropical Diseases, p. 713.

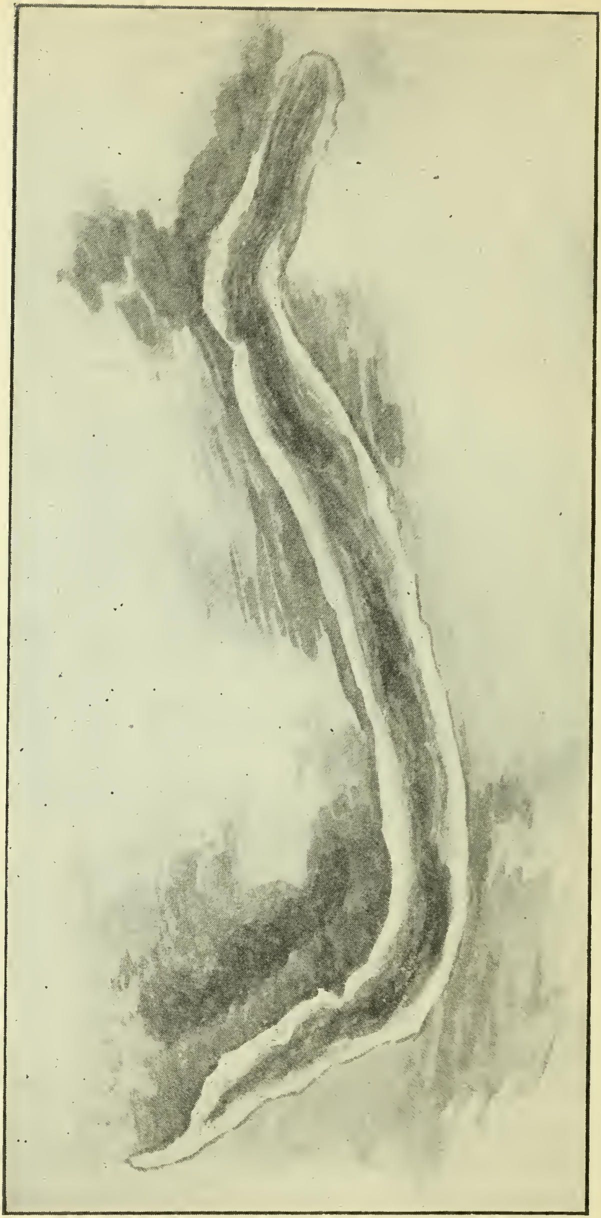

FIG. 9.—Entozoal embryo from fæces. Stain hæmatoxylin.

NOTE.—Figs. 3 to 9 are all drawn to the same scale for purposes of comparison.

(or more properly spirochæte) is considered by many observers to be a protozoan, and, in view of the theories of Schandinn and Zieman,[16] may eventually turn out to be a stage in the development of a flagellate. The possibility of relapsing fever being transmitted by ticks has recently been discussed by Ross and Milne, of Uganda.[17]

Trypanosomiasis.—I have made a persevering effort to find trypanosomes in the blood[18] with no result. I have not tried inoculation experiments. I have not found *Glossina palpalis,* but I have about 75 specimens of what I believe to be *G. morsitans* in my collection of biting insects. Mr. E. E. Austen, of the British Museum, author of A Monograph of the Tsetse Flies, has kindly identified for me the *Auchmeromyia luteola,* Fabr., which is a very common fly here as in other parts of Africa, and the anomalous blood sucking larva of which is possibly of interest in this connection.[19]

I reproduce here a series of blood examinations made in this district in 1903.[20]

TABLE II.—BLOOD EXAMINATIONS OF NATIVES.

Number of examinations for malaria	280
Number of cases where parasite was found	112
Number of cases showing excess of large mononuclears	91
NOTE.—When the parasite was found no differential leucocyte count was made.	
Number of examinations for filaria	300
Number of cases of filariasis	2
Number of cases showing eosinophilia	31

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[16] *Archiv für Schiff und Tropen-Hygiene,* 1902, Vol. vi, p. 389.

[17] *Brit. Med. Jour.,* November 26, 1904, p. 1453.

[18] I have not succeeded in getting natives to submit to lumbar puncture, so I have not examined the cerebrospinal fluid for trypanosomes. I have not yet tried the recent suggestion of aspirating the cervical lymphatic glands. (*Vid. Brit. Med. Jour.,* May 28, 1904, p. 1252).

[19] *Vid. Brit. Med. Jour.,* September 17, 1904, p. 664.

[20] Published in *Jour. Trop. Med.,* April 15, 1904, p. 123.

(2) DISEASES APPEARING FROM AN EXAMINATION OF THE FÆCES.

Dysentery (native name, *Pulukala,* from Portuguese verb *purgar*).—Porters, going from here to the coast for loads, often acquire this disease, which is endemic in the lower altitudes, and large numbers of them die from it. *Amœba coli* can sometimes be demonstrated in the fæces or mucus (as well as in the fæces of apparently healthy natives). I have never seen liver abscess. I have from time to time attempted to isolate a definite organism from the stools of cases in which no amœbæ were found. In two cases I found a bacillus which grew on the ordinary culture media. It did not liquify gelatin nor ferment glucose, and milk was not coagulated. It did not stain by Gram. Morphologically it resembled *B. typhosis* and *B. dysenteriæ,* Shiga. I did not test it for generation of gas, acid, indol, etc.

Ankylostomiasis (native name, *Apuka*).—Fairly common. Comparatively few ova can be demonstrated in the fæces. Under a two thirds object glass with No. 2 eye piece, one, or at most two ova will be seen in the field. The worms passed after thymol are also few. Nevertheless, the symptoms are sometimes very severe. There is often pernicious anæmia with many megaloblasts.

Ascaris lumbricoides (native name, *Olonyoha*).—Almost universal among children and a considerable proportion of adults are likewise affected. I once saw ninety-six worms passed by a child, 2 years old, the result of a single dose of santonine and castor oil. I have suspected for several years that there was a peculiar intestinal worm here that is very resistant to anthelmintics, and about a year ago I secured a specimen concerning which I wrote at that time as follows:[21] "I have a specimen of round worm, a female, passed by a white child, which is peculiar in having a deep constriction at a point about two fifths[22] of the distance from the head to

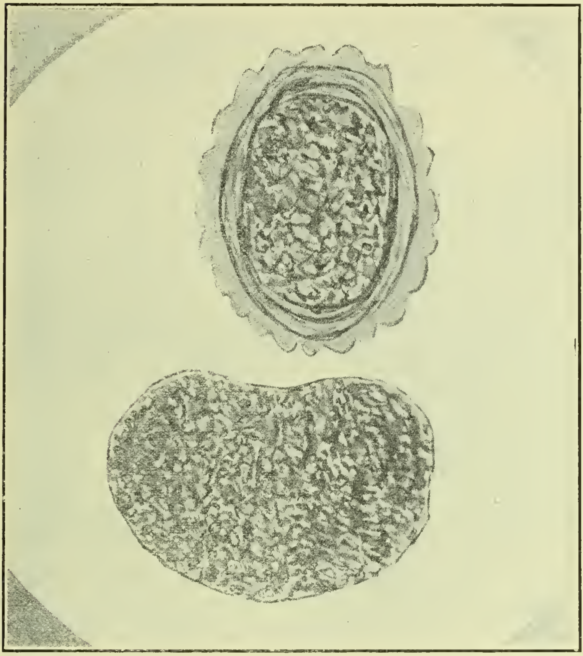

FIG. 10.—Ova of *Ascaris lumbricoides* and new species of *Ascaris* drawn to the same scale. Taken from uteri of parent worms and stained.

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[21] *Jour. Trop. Med.*, February 15, 1904, p. 53.

[22] This should have read "one third."

the tail, and corresponding to the sexual opening. In general appearance the worm otherwise resembles *A. lumbricoides;* but the ova seen both in the fæces and taken from the parent worm are, although about the same size, distinctly different from the ova of *A. lumbricoides* or *A. mystax.* They are bean shaped, and, in the mature form as found in the fæces, neither yolk nor shell can be made out. The crenated and rugose albuminous envelope is opaque and stained with bile, and might easily be mistaken for a small mass of fæcal matter. Ova taken from the uterus at various stages of development show a simple shell filled with a granular yolk." I have, since writing the foregoing, secured additional examples of this *ascaris,* and I think it possible that it may represent a new species or variety. The long, narrow egg with its opaque en-

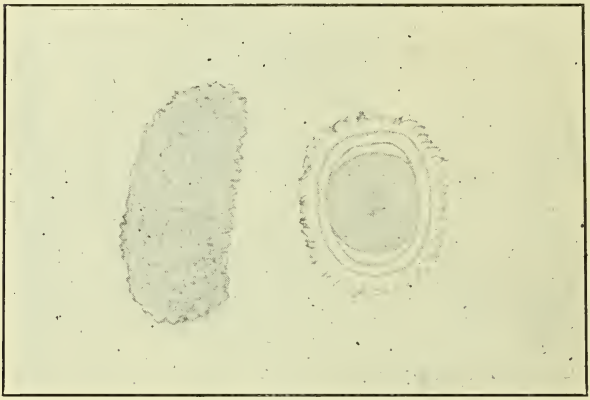

Fig. 11.—Ova of *Ascaris lumbricoides* and of new species of *Ascaris* as seen in fæces. Drawn to the same scale.

velope is strikingly different from a lumbricoides ovum.

Tænia (native name, *Apapi*).—I have seen examples of a bothriocephalus, *Tænia saginata,* and one specimen of a small cestode with marginal unilateral genital pores (*Hymenolepis sp.?*), of which I did not get the head. I also saw, in 1903, some fragments of what I thought might be a very small cestode entangled in vegetable matter in the fæces of a bad case of indigestion. I mounted some of these chains of what appeared to be minute proglottides and sent them to London; but they were unfortunately destroyed *en voyage*. Round (*tæniae*) and oval, operculated (bothriocephali) ova, as well as ciliated free swimming oncospheres, are occasionally seen in the fæces along with the ripe segments. Bothriocephalus infection gives rise to anæmia, that

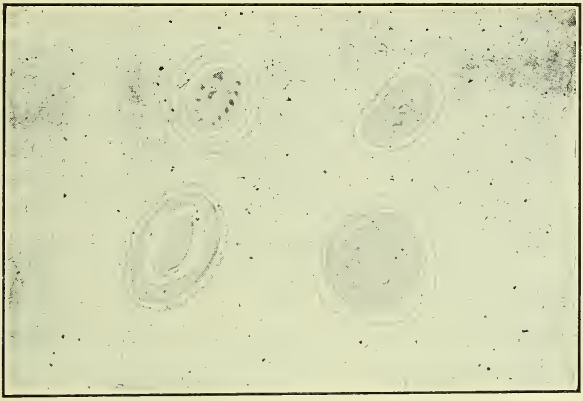

Fig. 12.—Ova of unknown entozoa seen in human fæces.

of tænia seems to cause the native little inconvenience.

Oxyuris vermicularis is common.

Tricocephalus Dispar.—Ova are seen, but are rare.

Schistosomum Hæmatobium.—Side spine variety of ova from fæces rarely encountered. Have seen one or two cases.

Chronic Diarrhœa (native name same as for dysentery).—Not infrequent. Intractable to treatment. I have sometimes seen it associated with enormous numbers of a small embryo which corresponds in some respects to the descriptions of *Aguillula, stercoralis.* It may be the embryo of a larger entozoon than *R. intestinale.*

Other Intestinal Parasites.—I have seen several cases of intestinal myasis. The domestic animals, especially pigs, are rich in entozoa more than a bare reference to which lies without the scope of this paper.

I append here the record of some fæces examinations made by me in 1903:[23]

TABLE III.—FÆCES EXAMINATIONS.

Number of fæces examinations	310
Number of cases of infection with lumbricoides	158
Number of cases of ankylostomiasis	13
Number of cases of Bothriocephalus latus	4
Number of cases of Tænia saginata	2
Number of cases of Anguillula stercoralis	2
Number of cases of Amœba coli	1

NOTE.—Daniels, from 251 fæces examinations in British Central Africa, obtained somewhat different figures—viz., lumbricoides, 15; ankylostoma, 25; tænia, 0; anguillula, 3 (*vide Journal of Tropical Medicine,* June 15, 1901, p. 199).

(3) DISEASES APPEARING FROM AN EXAMINATION OF THE URINE.

Hæmoglobinuric Fever.—Common among Portuguese officers, traders, etc., coming from the unhealthy littoral to the cooler highlands. Called by them "biliosa." The third attack is quite often fatal. I have never seen it in a native. I certainly believe it has some definite relation to malignant malaria. I should not care to say more than this; but antecedent malarial infection can generally be proved, its distribution in this country coincides with that of severe malaria, and I have twice seen large numbers of young malarial parasites in the blood of patients just taken ill with what afterward proved to be black water fever. Of course to demonstrate parasites the case must be examined early, as the vitiated erythrocytes containing the hæmamœbæ are the first to be destroyed when the terrific hæmolysis sets in. I have no doubt that a heavy dose of quinine[24] is as efficacious in provoking an attack as is chill, exhaustion, shock, or any other marked physiological disturbance. I have never seen black water fever in a subject in whom each attack of malaria was thoroughly and promptly treated. In regard to its distribution Stephens says,[25] "Black water fever is well known along the west coast of Africa, in Nigeria, in the Cameroons, in the Congo, *probably Portuguese West Africa, but whether as far south as Damaraland I am unable to say.*" (The italics are mine.) I can state that it is well known in all Portuguese West Africa to a point at least as far south as Mossamedes.

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[23] *Jour. Trop. Med.,* April 15, 1904, p. 124.

Endemic Hæmaturia (native name, *Ongandu*).—Bilharziosis is very common in some localities, rare or unknown in others. Ova of *S. hæmatobium* are plentiful in urine. I have not seen vesical calculi and new growths resulting from it, as is so frequently the case in Egypt. I have occasionally seen blood in the urine without apparent cause. These instances may be the result of hæmorrhagic bullæ which will be spoken of under local affections.

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[24] The Germans, following R. Koch, have in my opinion done harm by tacitly encouraging the neglect of quinine by the laity in tropical Africa. Cf. Fisch, *Tropische Krankheiten*, p. 93.

[25] Thompson Yates, *Lab. Report*, Vol. v, p. 200.

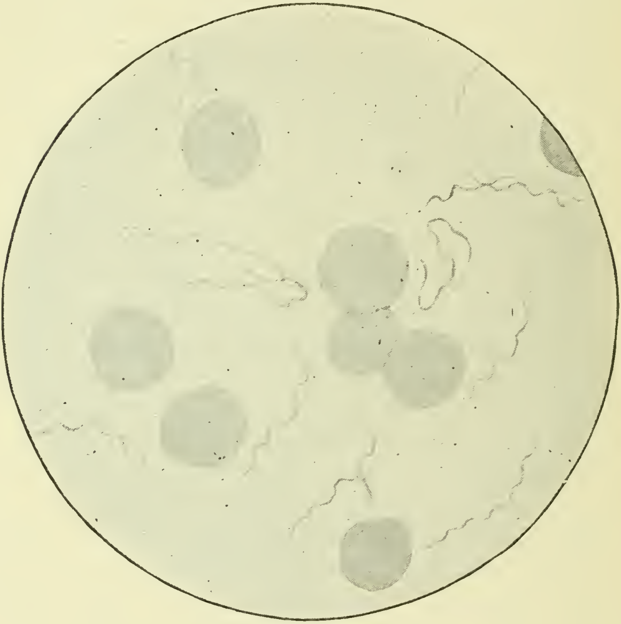

FIG. 13.

I published some time ago[26] the results of a few microscopical urine examinations, which I here submit:

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[26] *Jour. Trop. Med.*, April 15, 1904.

TABLE IV.—URINE EXAMINATIONS.

Number of urine examinations	72
Number of cases of bilharzia disease	3
Number of cases of filaria	1

(4) DISEASES APPEARING FROM AN EXAMINATION OF THE SPUTUM.

These are almost *nil.* I have seen cases among natives closely simulating *Tuberculosis pulmonalis,* but a careful examination of the sputum always negatived the diagnosis. In this equable climate even the scourge of the aged, chronic bronchitis, is rare and mild. I have not found any sort of distomum in sputum. There is, however, a distinct and peculiar affection of the chest very common throughout the whole country. The native name is *Vonulo.* I have already mentioned this disease in a former article,[27] but as it seems to be unique I propose to describe it briefly here. In my former note I contented myself with naming the more striking symptoms of the disease, comparing it with asthma and suggesting that it might be the manifestation of a neurosis. Since then I have given some time to the further observation of the condition and now present the results of this fuller study.

Name.—The native name, Vonulo, signifies pain in the chest. But they carefully distinguish it from pains in the chest due to bronchitis, pleurisy, cardiac affections, etc. Vonulo is *the* pain in the chest not *a* pain. I should suggest, as fairly descriptive, the term *Sternodynia neuralis endemica.*

Definition.—A nervous affection of the bronchi and bronchioli depending on a peculiar diathesis.

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[27] *Jour. Trop. Med.,* February 15, 1904, p. 54.

It is characterized by constant pain under the sternum, which is often worse at night. Mild cases occur. The trouble sometimes disappears spontaneously for long periods or permanently.

Geographical Distribution.—I should be inclined to say that the disease is to be found throughout the district occupied by the Umbundu speaking highlanders. While I have not, of course, been all over such a district, yet in all the various localities I have visited the first inquiries have been for medicine that would relieve vonulo; and I have had patients with it from literally every part of the country.

Frequency.—This is a matter upon which it is hard to pronounce. At most such a question is purely one of judgment. I should place it at 6 to 8 per cent. of the population in the localities where I am acquainted. This estimate includes mild cases.

Economic Importance.—This is not inconsiderable. Of course there is malingering. The acknowledged existence of a disease with neither objective symptoms nor a visible anatomical basis offers a loophole of escape from government duty, etc., which the astute savage does not fail to utilize whenever possible. When it is known that a settlement of 1,500 whites (to say nothing of mulattoes and civilized blacks and of other settlements farther inland) is dependent on porters for supplies from the coast 300 miles distant, some idea of the economic significance of the disease is gained.

Ætiology.—Obscure; I have not done more than satisfy myself that it is not caused by an obvious zooparasitic invasion. In one case I saw a large diplococcus in the sputum. I made cultures from the scanty sputum in several severe cases. I got staphylococci, a long, slender bacillus, probably *Leptothrix buccalis,* etc. There is almost no sputum and my cultures were, therefore, practically all made from saliva, and I have attached no importance to anything found so far.

Symptomatology.—Severe pain, sometimes of the shooting variety, in the chest, generally under the sternum, occasionally accompanied by pain under one or both shoulder blades. The temperature and pulse are generally unchanged. Respiration is often shallow and somewhat accelerated. Sometimes there is a feeling of constriction, but never marked dyspnœa. Aching, which is often worse at night; rarely throbbing and tenderness. These symptoms are aggravated by running, carrying loads, and other violent exercise. Of course pains in the chest from other causes are sometimes mistaken both by the patient and medical man for vonulo, but after liberal allowance is made for this margin of error, there remains an enormous number of cases which can only be accounted for by predicating a specific cause for these constant symptoms.

Diagnosis.—This presents few difficulties. Following is a comparison of vonulo with some of the conditions for which it might possibly be mistaken. (1) From asthma: no dyspnœa, attack not sudden, not limited to spasmodic attacks, little or no wheezing, no forced expiration as in asthmatics, asthma unknown here except in occasional newly arrived whites. (2) From pleurisy: does not run an acute course, character of pain different, patient does not assume position of one with plastic pleurisy, no loss of respiratory motion, no dullness, no friction sounds, no effusion. A severe case resembles interstitial pleurisy more than any other form, but there is no cough, no hæmorrhages, and the fearful dyspnœa which is characteristic of that disease is absent. (3) From chronic bronchitis: generally no cough or expectoration, no bronchiectasis. (4) From angina pectoris: not paroxysmal, does not supervene on sudden exertion or strong emotion; the pain is much milder (there is neither the intense *dolor pectoris* nor the *angor animi*). (5) From hepatitis and liver abscess: lack of enlargement and tenderness, no history of dysentery, no rigors or night sweats, observation of decubitus. The pain under the shoulder which occurs in both diseases might cause confusion were it not that liver abscess is extremely rare, if present at all, in this region. (6) From splenitis: hundreds of cases occur in which the spleen is normal. (7) From endemic hæmoptysis, tuberculosis, actinomycosis, hydatids, etc.: in these days of routine microscopical examinations no one who pretends to be *au courant* with his profession would neglect to look carefully into the character of the sputum when studying a chest affection.

Prognosis.—Good as to life, uncertain as to relief. The pain, loss of sleep, etc., are especially hard on elderly natives. While never the immediate cause of death, vonulo is one more of the many factors which weaken the powers of resistance and invite intercurrent affections.

(5) DISEASES APPEARING FROM AN EXAMINATION OF THE SKIN.

Leprosy (native name, *Ovihata*).—Ovihata is a loose term including different skin affections. Leprosy is becoming distinctly more common in this immediate vicinity during the last eight or ten years. In one group of villages, where there was one leper seven years ago there are half a dozen to-day, and a similar condition obtains in other groups. No attempt at segregation is made by the natives or the Portuguese authorities. Nerve leprosy is the more common form, which appears to be rather anomalous in a country where leprosy is comparatively new. In early cases I have seen the bacillus in preparations of the nasal discharge stained by Ziehl Neelsen's method. I have encountered a few cases of the nodular variety. One of these I had an opportunity to examine histologically. The general histological architecture was that of the infective granulomata with the addition of large bundles of *Bacillus lepræ* scattered through the sections.

Yaws (native name, *Ohumbula*).—Fairly common, although I doubt if it is endemic. The natives generally acquire it in the Luba district of the Congo Free State, where they go slave trading. It is attributed by them to sexual promiscuity with the Luba women. The blacks believe there are two varieties of yaws, one characterized by large and the other by small sores. Cases generally are typical. I believe it is entirely distinct from syphilis. I know of one white man who contracted it.

Multiple Fibromata (native name, *Olombulu*).—I have seen several cases of these. I have now in my employ a native, the greater part of whose body is covered with little tumors, ranging from the size of a small pea to that of a marble. They are sessile and movable. They do not seem to interfere with the general health. Sections made of the tumors look, under the microscope, like white fibrous tissue.

Craw-Craw (native name, *Olohala*).—Scabies, from the mildest to almost incredibly severe and neglected cases, sometimes present any and all the symptoms enumerated in descriptions of this disease. I have not found filariæ in the papules. The itch parasite (*Sarcophytes scabei*) can almost always be found.

Ringworm (native name, *Ocindamba*).—There are ringworms here, but I do not know what fungi cause them, as I have not yet found leisure to study them.

Prickly Heat.—Seen only among Europeans.

Leucodermia (native name, *Uyamba*).—I have called my cases leucodermia rather than pinta for the following reasons: (1) The patches are always of one color, white.[28] (2) There is little desquamation. (3) The patches are not itchy. (4) I have found nothing like mycelial filaments in the scales. (5) The pigment changes are comparatively slight.

Ukau (a native name).—A skin disease resembling eczema.

Ovilundu (native name).—An epiphytic disease somewhat resembling *Lupus vulgaris* in its macroscopical appearance.

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[28] The white variety of Pinta is associated with patches of other colors. Cf. Brault, *Traité pratique des maladies des pays chaude et tropicaux*, p. 282.

NOTE.—The native names of the three last diseases are the same as three varieties of edible mushrooms, and the native notion is that the diseases are caused by eating and handling the several mushrooms. The tropical diseases caused by epiphytes deserve more attention than they have yet received.

(6) DISEASES DETECTED BY A GENERAL EXAMINATION OF THE BODY.

Beri-Beri.—Rare in this particular locality. I have seen only two cases here. In other parts of Portuguese West Africa it is very common, especially in the island of St. Thomas. When I visited the School of Tropical Medicine in Lisbon a few months ago I was shown several typical cases in white soldiers and sailors who had seen service in this colony, and I have heard of a number of naval and military officers who have been invalided home with it.

Sleeping Sickness.—Does not occur in this immediate district, but is a scourge in some parts of the province. Have examined three cases here, all of which came from the Lunda district, to the north of here, beyond the Coanza River. I at one time spent several months at Malange, Lunda district, where I saw many cases, the disease being very common there. I have never known of a well authenticated case originating here.

Low Fever (native name, *Ocipuiyi*).—Common both among whites and natives. Thought by the latter to be caused by fatigue. Oftenest seen in new arrivals and infrequently mistaken by them for malaria. I believe there are several unclassified atypical fevers here. The matter needs study.

Heat Stroke.—Rare. I have met with two cases, both of simple heat exhaustion. The first of these was that of an American missionary about 60 years of age. The other was my own experience. I suffered a stroke in 1902. The case exhibited almost exactly the symptoms detailed by Manson.[29] Since then I have adopted the suggestion of a red covering for head and spinal region when compelled to be long in the sun, which affords great relief. While my symptoms were those of heat exhaustion rather than those of sun traumatism, yet I find since that, unless so protected, I feel the sun's rays more than formerly.

Akatama (a native name).—This is an endemic neuritis which I have already described in another place.[30] I have examined hundreds of natives with it and have made and have by me notes on a number of these cases. Akatama is distinct from beri-beri, from malarial neuritis, from the peripheral neuritis sometimes following dysentery, etc., and, so far as I can learn from other described diseases, including the different tropical neuroses. The following description is partly copied from the former article just referred to.

The foregoing name given the disease by the natives is, contrary to the general rule, without significance. Native names for diseases are usually descriptive. The name I have used in keeping my records is *Neuritis peripheralis endemica.*

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[29] *Tropical Diseases*, p. 284.

[30] *Jour. Trop. Med.*, September 1, 1903.

Definition.—An endemic peripheral neuritis of obscure origin, characterized by numbness and intense prickling and burning sensations in the presence of cold or damp, which are temporarily relieved by the application of dry heat.

Economic Importance of the Disease.—While the trouble affects young and old, male and female, the economic significance of it lies in the fact that good porters and servants are rendered inefficient by it, often to the hindrance of necessary work. An otherwise good porter would rather receive a beating than start out with akatama before the sun is high. He hangs over the fire mornings and on rainy days. Conversely a servant absolutely worthless on a cloudy day may give his usual service while the sun is shining or while he can be employed near a fire. Akatama is found oftener in men than in women, in the young and middle aged than in the old, and not at all in children and Europeans.[31]

Frequency.—I should be inclined to say that from three to five per cent. of the population are affected.

Ætiology.—Locally I have found nothing that throws light on the cause of the disease. I give here a digest of the notes of a study, made in 1902, of a series of thirteen typical cases which I kept under observation for some time.

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[31] I have never seen the disease in a Caucasian, although I examine a number of officers, missionaries, traders, etc., every year.

Table IV.—Blood and Excreta of Thirteen Patients Suffering from Akatama.

	Blood.			Fæces.			
No. cases.	Presence of malaria. * Plasmodium.	Dif. Leuc. count.	Filiariasis.	Ascar. Lumb.	Ankylos. D.	Tænia.	Urine.
1	....	...	...	...	...	...	....
2	Malig. ter., ring form.	...	...	Yes	...	...	Albumen.
3	....	†Yes	...	...	...	...	....
4	....	Yes	...	...	...	...	....
5	Malig. ter., ring form.	...	...	...	...	...	Bilharzia hæmatobia.
6	....	...	...	Yes	...	Yes	....
7	....	Yes	F. perstans	Yes	...	...	....
8	....	...	...	Yes	...	...	....
9	Malig. ter., ring form.	...	...	...	Yes	...	....
10	Malig. ter., ring form.	...	...	...	Yes	...	....
11	....	Yes	...	Yes	...	...	....
12	....	...	...	Yes	...	...	....
13	....	...	...	...	...	...	....

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* When the parasite was found no count of leucocytes was made.

† *I.e.,* mononuclears 20 per cent. or over.

I take it that the filariasis, ankylostomiasis, and bilharziosis were adventitious, and of course the malaria is to be taken for granted. So I should be inclined to say, after using as control statistics of examinations made for other purposes, that the table represents a fair average of the natives in the district, and that careful and continued observation of any similar group would reveal practically the same conditions with the possible exception of the filariasis and bilharziosis, which are comparatively rare. In one or two cases where there was cough I likewise examined the sputum, but with negative results. While I hope to make at some future time a more extended inquiry into the ætiology of akatama, I should say meanwhile that no obvious universal cause is apparent.

I have proposed to myself a number of theories to account for the symptoms. Some of the most probable seem to be: (1) That akatama is caused by exposure to sudden changes of temperature, e. g., from warm sun to cold rain, and especially from the warm sand of the paths into cold streams. Also the great change from the cool mornings and evenings to the heat of the day. This is the idea of the natives themselves. The fact that the trouble first appears on the most exposed parts, i. e., arms and legs, seems to support this hypothesis. Against it appears the fact that girls, cripples, the aged, besides others who are little exposed, also contract the disease. (2) Another theory is that akatama is an intoxication analogous to beri-beri. This intoxication might be from organisms in food or soil, or it might be accounted for by the fact that the maize eaten is always allowed to partially ferment at a stage in the process of preparing it for food. In a case with pretty general implication of the surface of the body this idea impresses one reasonably. When the trouble is confined to a small part of the body a local cause seems to fit the facts better. Again, there are no motor symptoms. I do not find that akatama is a "place disease" nor that change of residence necessarily has any effect on it. (3) A third theory is that the symptoms are the result of nerve starvation, as the natives are a poorly fed people. This is not borne out by the facts. Chiefs, the rich, and the well fed suffer alike with the poor;

and treatment founded on this last supposition has not succeeded in relieving the symptoms.

Pathological Anatomy.—While there is found during the exacerbations of pain, etc., some swelling, erythema, and, in bad cases, slight œdema, which may persist for a little while after the spasm has passed, yet neither macroscopical nor microscopical inspection reveals anything either of neuromata or of connective tissue change. Sections and teased preparations of nerves from a patient who died from the effects of an accident showed none of the characteristic changes found in the nerves of old beri-berics. Yet the severity of the symptoms and their character indicate that akatama is a true neuritis and not a neurosis. Further work with the microtome may show organic changes which I have overlooked.

Symptoms.—(1) Subjective: Shooting, prickling, "crawling" pains in the affected parts accompanied by numbness. These are relieved by the heat of the sun or a fire. The combination of wet and cold seems to greatly intensify the suffering. Patients often say, "When I step on a cold, damp place it is awful." (2) Objective: The erythema is of course particularly noticeable on light colored natives. There is often some swelling, which as a rule quickly subsides as the patient gets warm over a fire or in the sun. Excessive sweating of the part sometimes occurs. These symptoms generally appear on the legs and forearms, sometimes on the thighs and arms, and occasionally on any part of the body or all over the body. In severe cases the walk is peculiar—a tendency to curl the toes as if walking on the heels and ends of the toes. I have seen several bad cases, the sufferers from which could not walk at all in cold weather.

Diagnosis.—The diagnosis is easy. There are a few things for which akatama might be mistaken. (1) From Strachan's disease:[32] Nerves of special sense (sight, hearing, etc.) not affected, no wasting of muscles, no vesicles along track of nerves with subsequent desquamation, no excoriation of mucocutaneous orifices, no motor symptoms. The only common manifestations are the numbness, burning, and hyperæmia. Strachan's disease is a multiple neuritis, akatama is a peripheral neuritis. (2) From beri-beri: No pain in the calves, lumbar region, etc., on pressure, no heart symptoms, œdema slight and transitory (not always present) and no atrophy. The peculiar walk is from the pain and is very different from the beri-beri walk. The reflexes are normal and there is no ankle drop. From other paralyses: The limping walk is not always the same. It is sometimes on one side and sometimes on the other. It is not ataxic and is a transitory symptom. (4) From elephantiasis: The swelling in akatama is slight and transitory and the part returns to its normal size after the attack. No rise in temperature as in lymphangeitis, and examination of the skin shows no structural changes. (5) From leprosy: Absence of bacilli from nasal discharge, etc., lack of anæsthesia, sweating of affected part, no pale spots or nodules. (6) From malarial neuritis: By examination of the blood, spleen, etc. Not amenable to quinine. (6) From neuritis following dysentery, etc.: By the case history.

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[32] *Vid. The Practitioner*, November, 1897, p. 477.

Prognosis.—Good as to life and health, uncertain as to relief. The trouble sometimes ceases spontaneously after years of suffering.

Pellagra.—Dr. Sandwith, of Cairo, asked me last year in London to determine the presence or absence of pellagra in South West Africa. I have accordingly had the matter in mind, but have not yet seen the disease. I examined some maize when I was making my studies of akatama, but did not find any of the moulds which are common in Egypt, Italy, etc. (*Aspergillus fumigatus, A. flavisceus*, and *Penicillum glaucum*). The corn is always well dried here before storing.

Manioc Poisoning.—There are two kinds of manioc grown by the natives, called by them "sweet" (*Manihot utillissima,* Pohl) and "bitter" (*M. aipi,* Pohl). These are sometimes confused, especially by children, and consequent poisoning results. This only occurs when the root is eaten in its raw state, as both are harmless when cooked.

Poisoning by Witch Doctors (native name, *Owanga*).—This frequently takes place. Among the substances often used for this purpose are the rootlets of a small tree with minute simple leaves (*Securidaca longipedunculata,* Fres.), and the powdered bark of a graceful tree with sweet smelling flowers (*Erythrophlœum guinense,* Don.). This latter causes paralysis of the heart and is one of the principal ingredients of the poison test employed by the natives to settle disputes among themselves. The natives are sometimes frightened to death by these witch doctors. The *modus operandi* is to curse the devoted one, prophesying his early death, etc. The victim generally gives up hope and dies on the very day named. Of course poison is often secretly administered along with the curses; but some cases are, beyond a reasonable doubt, mere fright.

(7) LOCAL AFFECTIONS.

Hæmorrhagic Bullæ (native name, *Onyalai*).—This complaint, the occurrence of which in this district I pointed out some time ago,[33] is a frequent and very treacherous disease greatly feared by the natives. Considered by them very fatal. I was once disposed to treat the native view very lightly, but, after seeing cases die from it in a few hours from the beginning of an attack, I revised my notion. The bullæ may be small and affect only the surface of the body, or occur only on the tongue, soft palate, or buccal mucus membrane. When large and involving the œsophagus they may cause trouble, but when they occur in the brain, its membranes or even the important abdominal viscera, death often results. The disease is not pemphigus, *Dermatitis herpetiformis* nor the affection known as *Epidermolysis bullosa.* The bullæ appear suddenly after an initial period of malaise. They range in size from that of a split pea to that of a silver half dollar. The larger ones are occasionally somewhat sunken in the centre. The vesiculation is rather deep and, when occurring in the skin, always involves the corium. The bullous formations contain trabeculæ, the interstices of which are filled with partially coagulated blood, to which their dark color is due. The disease generally disappears (if death does not occur) as suddenly as it came. I have heard of similar affections from East Africa and from South China. Dr. A. Y. Massey has recently published a report of three cases from West Africa.[34]

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[33] *Jour. Trop. Med.*, February 15, 1904, p. 53.

Marginal Ulceration of the Gums.—Sometimes spoken of by the laity as "land scurvy" (native name, *Ocimumusu*).—Quite frequently seen. Causes loss of teeth and secondary anæmia if not treated. Is distinct from ordinary *Pyorrhœa alveolaris.*

Velda Sore (Delhi Boil?).—What partially corresponds to the descriptions of this trouble occasionally occurs in the form of small epidemics. I stained some scrapings by Leishman's and by Van Gieson's method, but failed to see anything which resembled my specimens of *Leishmania donovani.*

Climatic Buboes (native name, *Owanbe*).—There are of course enlarged glands from various causes which are not Climatic Buboes; but I am inclined to think some of my cases are these latter.

Keloids (native name, *Ocimbusi*).—Keloidal fibromata of ears, etc., are common. The native seems to have a tendency to keloidal formation. Scars from burns, tattoo marks, etc., often take on this character. Histologically they are a true hypertrophy of the white fibrous tissue.

Goître (native name, *Esasa*).—Remarkably common, especially among women. Rarely it reaches an enormous size, twice or even three times as large as the person's head. I have not observed that goître is more frequent in regions lying along rivers, and it certainly has no relation in this country to residence on calcareous soil.

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[34] *Jour. Trop. Med.*, September 1, 1904, p. 269.

Tropical Phagedæna.—Not so common here as in lower altitudes. Generally attributed by the blacks to some small injury.

Ainhum (native name *Ombanja*).—Occasionally causes pain and inconvenience enough to bring patients for surgical intervention.

Jigger (native name, *Ewundu*).—The *Sarsopsylla penetrans* is a universal pest here. It was introduced into this colony (by the Portuguese from South America) about thirty-five years ago. Since then it has nearly traversed the continent and is steadily pursuing its way around the world. Shocking deformities, gangrene, and blood poisoning may be mentioned as some of the evils for which the jigger is often responsible.

Myasis.—Have seen but two cases of "screw worms." One of these occurred in a white child, the other in a dog. Said to be commoner on the coast than here. I have not succeeded in capturing the imagoes, commonly called Mangrove flies, of which I have the larvæ. I have specimens of a fly not yet determined, which possesses the metallic thorax and abdomen, bristled mid-tibiæ and palpal features of the genus *Lucilia;* but I do not know its life history. There is also here at least one species of the genus *Sarcophaga,* which Mr. Austen, of the British Museum, provisionally informs me is *regularis,* Wied., or a species near it. I have watched this fly depositing its living larvæ on fæces, decaying meat, and wounds. There are also several species of flies with plumose arista, metallic abdomen, and dark thorax (*Calliphora?*) which are the common cause of maggots in neglected wounds. I have never seen the larvæ of flies in the nostrils or eyes of natives, who, nevertheless, continually sleep in the open air. Intestinal myasis has already been mentioned.

Snake Bites.—The worst and commonest of poisonous snakes is the *Ombuta,* a puff adder. Its bite is fatal unless treated. Ophidism is rarer than one would expect in such a country.

Other Bites, Etc.—I have found the following vermin of man: *Pulex irritaus, Pediculus capitis, P. vestimentorum* and *Acanthia lectularia.* I have collected several species of ticks, most of which have not yet been determined. I may speak here of the *Ocihopis* (*Ornithodorus moubata*). This acarus is never lacking in old native huts. Its bite is very painful, as I can personally testify, the swelling and irritation not subsiding for days. However, I cannot say that I have definitely recognized tick fever as the result of this ixodiasis. It is not improbable that so called tick fever and relapsing fever are identical, as has already been pointed out, although the exact mode of transmission has not been observed. There are several poisonous centipedes. A large myriapod, which does not bite, is greatly feared on account of the intense smarting and burning which it leaves in its wake as it crawls over the surface of the body. The track left looks like a burn from a hot iron drawn across the skin. There are at least four varieties of hornets. One of these, a reddish, striped one, stings terribly. A large black ant three quarters of an inch long, which marches like the ordinary driver ant (*Anomma arcens,* West.) in military order, is said to have a sting that is as severe as the bite of a poisonous snake. A battalion of these ants on a foray make, when disturbed, a loud, vicious, buzzing sound. Scorpions are unknown in this particular locality, but are common in other districts. I have already spoken of mosquitoes, the tsetse flies, and the larva of *Auchmeromyia luteola.* Of the other biting diptera the genus *Hæmatopota,* of which I have found four species, is the commonest. One of these has been sent to Mr. Austen, who believes it may represent a new species. I am sending specimens of the others at this writing. The *Tabanidæ* thus far collected are represented by two species, one of which Mr. Austen thinks may be new, and which is near *T. latipes,* Macq., and the other *T. rubricundus,* Walk., or a closely allied species. I have also taken a single species of *Stomoxys.* Mr. Austen's determinations given must be regarded as tentative, as I have not yet received his report.

Leeches (native name, *Etuli*).—I have heard of exhaustion from loss of blood by these when carriers are forced to traverse large swamps and plains covered with water.

Eye Troubles.—Ulcer of cornea (native name, *Onende*) sometimes seen. There is much blindness as a result of smallpox. Trachoma is rare. I have not seen *Filaria loa.* Quinine amblyopia has been observed several times. Contagious "sore eyes" (acute mucopurulent conjunctivitis) comes around every two or three years. I have had no occasion to concern myself with the errors of refraction occurring in natives.

APPENDICES.

(*A*) *Epidemics.*—Smallpox (native name, *Ocingongo*).—There have been two epidemics of this scourge during the past eight years.[35] Numbers of natives were carried off by it. The blacks do not believe in adopting any measures against it. Many mild cases occur. I have seen cases so slight as to present only one pustule. There is little secondary fever and the mortality is low. I vaccinated one community of about 250 natives, among whom not a case occurred.

Chickenpox (native name, *Osalambu,* from Portuguese Sarampo, measles, the natives having mixed the names).—Two epidemics occurred in eight years, nearly synchronous with the smallpox epidemics just mentioned. The natives believe smallpox is always preceded and caused by chickenpox.

Mumps (native name, *Okapukulu*).—One epidemic in eight years.

Influenza (native name, *Ocisinda*).—One partial epidemic.

Whooping Cough.—I have heard of one or two local epidemics of what may be this disease.

(*B*) *Other Diseases Occurring in All Climates Which Obtain in This District.*—Epilepsy (native name, *Ocinonya*).—Very common. In children it must be distinguished from the convulsive type of malaria and from the fits caused by Ascariasis. Considered by the blacks a contagious disease.

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[35] Ocingongo differs in some respects from varioloid. It is not, however, modified chickenpox, but is closely allied to smallpox. It resembles regular varioloid more closely than it does the epidemic varioloid varicella of Jamaica (*vid. Trans. Epidem. Soc.*, Lond., Vol. ii, p. 414). It has many points in common with the "Amaas" or Kaffir milkpox, described from South Africa (*Lancet*, May 7, 1904, p. 1273).

Pneumonia.—There is a pneumonia here which is occasionally fatal.

Chronic Bronchitis.—Sometimes seen in the aged. Generally mild.

Spermatozemia.—Common among polygamists with many wives.

Chronic Cystitis, Etc.—Bladder troubles, other than bilharziosis exist, but I have not given them more than general attention. The bacteriology of the urine in the tropics has been little studied and should present a fruitful field for investigation.

Gonorrhœa and Syphilis—Have been introduced from the coast by whites and civilized blacks. They are on the increase.

Rhachitis.—Occasionally seen.

Mental Diseases.—Rare.

Heart Affections.—Very rare.

Paralyses.—Sometimes seen.

Typhoid fever and rheumatism are, I believe, unknown, in this immediate district at least.

(*C*) *Surgical Affections.*—A vast number of surgical cases never apply to the European practitioner, preferring native treatment. I append a list of the troubles from which I have received applications for relief.

Cataract (native name, *Olohopio*).—Not uncommon in the aged. I have an impression that cataracts here are larger and harder to deliver than at home. At any rate I believe in raising a rather deeper flap than I was taught at the Royal Ophthalmic Hospital. I should say one needs all the room afforded by a flap consisting of fully half the cornea.

Hernia.—Inguinal hernia is not rare; umbilical hernia is amazingly common.

Deformities Generally the Result of Accidents. —Not frequent.

Tumors Other Than Keloidal.—Rare.

Malignant Growths.—Exceedingly rare. I have known of only one or two authenticated instances.

Bone Necroses.—Fairly common. Sometimes the result of deep ulcers.

Abscesses.—Small abscesses very common. Have seen several cases of abscess of the spleen, one of which I have published.[36] I have already mentioned that abscess of the liver is apparently unknown.

Laceration of the Cervix Uteri.—Result of too early child bearing. Often gives the patient little or no trouble.

Bites of Animals.—Have seen 14 cases of natives mauled by lions and leopards. I have reported one case of a boy who was severely injured by a leopard.[37]

Gunshot and Other Wounds.—These are generally brought to the "White Doctor," so I see a considerable number.

Fractures.—Oftenest of the femur.

Minor surgical cases of various kinds are many.

In conclusion I may again say that the foregoing outline does not pretend to be exhaustive. The most claimed is that the data given have, almost without exception, come under the personal observation of the writer. I have not felt justified in venturing opinions on many isolated and obscure cases which have fallen under my notice. The method adopted is, it should be remembered, rather practical than academical, and in the matter of nomenclature I have not sought to be rigidly consistent, but have chosen those terms most generally employed. I have regarded the parasitic and other diseases of animals (which are many and of great interest) as lying outside my purpose in writing this article, and have excluded for the same reason discussion of the native remedies for various diseases. I hope to consider these questions later. One interesting point brought out by this survey is the probable absence of bubonic plague, cholera, and yellow fever. *Cæteris paribus*, one would expect to find at least one representative of such successful and cosmopolitan tropical diseases as these in a country which is so admirably adapted for breeding them as in Southwest Africa and which is visited by ships from all over the world. Another point is the existence of two diseases (*Akatama* and *Vonulo*) which seem to be either peculiar to the place or to have thus far escaped notice in other regions. Of course it is possible that these are only modified clinical pictures of described diseases which I have failed to recognize; but they have seemed to me distinct conditions, and I have accordingly devoted comparatively large space to their description.

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[36] *Jour. Trop. Med.,* April 15, 1904, p. 125.

[37] *Ibid.,* p. 124.

I could wish that the preceding pages were a more worthy contribution to the geographical distribution of disease; but to those who have practised in the tropics it is not necessary to detail the varied hindrances to observation and study that have prevented my making the review more complete. I should like, too, to have some of my observations and experiments repeated and my conclusions tested by other observers. I trust, however, that this brief conspectus of the more obvious disease conditions in a little known district may be of some interest, and possibly serve as a nucleus to which may be added the results of further work.

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The American Society of Tropical Medicine.

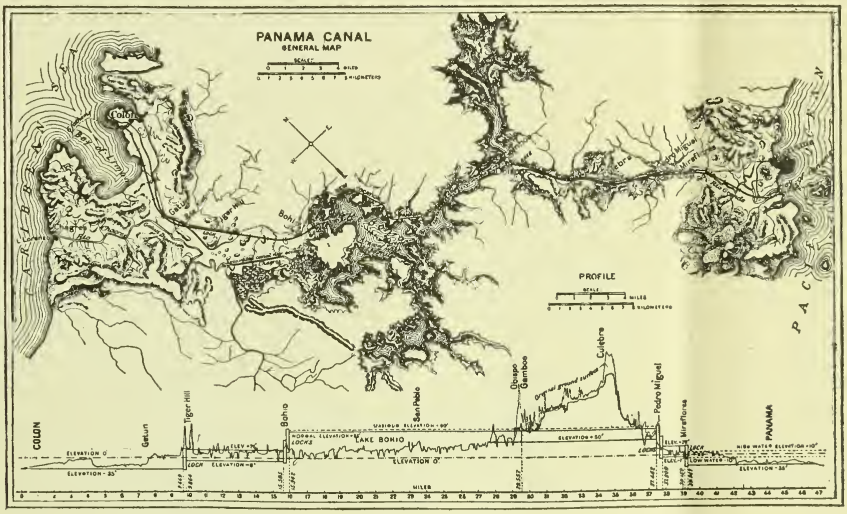
1905.

THE HISTORY OF PANAMA AND THE PANAMA CANAL.[1]

BY SENECA EGBERT, M.D., PHILADELPHIA.

Any history of Panama must naturally include, on the one hand, an account of the Isthmus and its capital city, and, on the other, the story of the interoceanic railroad and canal that have attracted so much of the world's attention during the past fifty years.

Vasco Nunez de Balboa has the credit of the discovery of the Pacific Ocean in 1513, but it may interest some to know that he had visited the Atlantic side of the Isthmus at least a dozen years earlier, and that he and his compatriots had founded Santa Maria de la Antigua—the first European community on the continent—in 1510. All trace of this settlement has long since disappeared, and Panama, which was founded almost ten years later by the father-in-law of Balboa, Pedro d'Avila, now claims to be the oldest American city. Strictly speaking, even this is incorrect, for d'Avila's stronghold was six or seven miles from the present site, and was burned by Morgan and his buccaneers in 1671, the present city being founded by Villacorta in 1673.



Map of the Panama Canal Zone, copied from the "New International Encyclopedia."

During the seventeenth and eighteenth centuries this city, old and new, was a port of great importance in Spain's trade on the Pacific, and was the gateway through which passed most of the gold and silver from Peru after Pizarro's conquest of the Incas. At the time of Morgan's raid the old city had several thousand inhabitants and "eight monasteries, a cathedral and two churches, a fine hospital, 200 richly furnished houses and 5000 of a humbler sort, a Genoese chamber of commerce, and 200 warehouses," of which the ruins of only one church now remain. As one writer says: "Then Spain was at the very zenith of her fame and wealth, and in Old Panama the splendor of the mother country was reproduced. With the pearls of the islands, the gold from Darien and the coast of Central America, and the silver of Mexico and Peru, it was rich to a degree. It was a life of luxury, of Spanish pleasure and dash, almost Asiatic in character. The Vice-Regal Court was grand and imposing; proud and brave noblemen surrounded the Viceroy, who was kingly both in power and surroundings. People those highways with richly dressed noblemen attending Spanish women whose beauty is historic, mounted on their Andalusian chargers and attended by a suite of followers. The very atmosphere down there seemed to teem with the music of old-time bells. To-day not a house remains intact. That city, then considered the Key of the Pacific and the Gate to the Universe, is silent and overgrown by a dense tropical forest over two hundred years old."[2] No wonder Morgan thought its treasures worth the arduous trip across the Isthmus, especially as his appetite had already been sharpened by the capture and looting of Porto Bello and Chagres, the former of which was then the Atlantic port of Panama, and both being strongholds of considerable importance.

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[1] Read at the annual meeting of the American Society of Tropical Medicine, March 24, 1905.

View of the harbor and part of the city of Panama, from the balcony of the President's palace.

Almost all histories unite in telling us that Panama is an Indian word, meaning "a place abounding in fish." They might also have defined it as one "abounding in *graft*." Doubtless Balboa and d'Avila, the founder, and many of the residents of the old city were well versed in the "science." The rich loot that Morgan's freebooters carried off was graft for them, for is not its essential principle embodied in the dictum that "to the victor belong the spoils?" We can be sure, too, that graft entered into the building of the new city, for we are told that the walls alone cost over eleven million dollars, and at a time when labor of the cheapest was to be had. It is said that one day the King of Spain, gazing from his palace window to the westward and shielding his eyes with his hand, remarked to one of his ministers: "I am looking for the walls of Panama, for they have cost enough to be seen even from here." What would he have said could be have known of that climax of graft that was to be developed in the same vicinity two centuries later?

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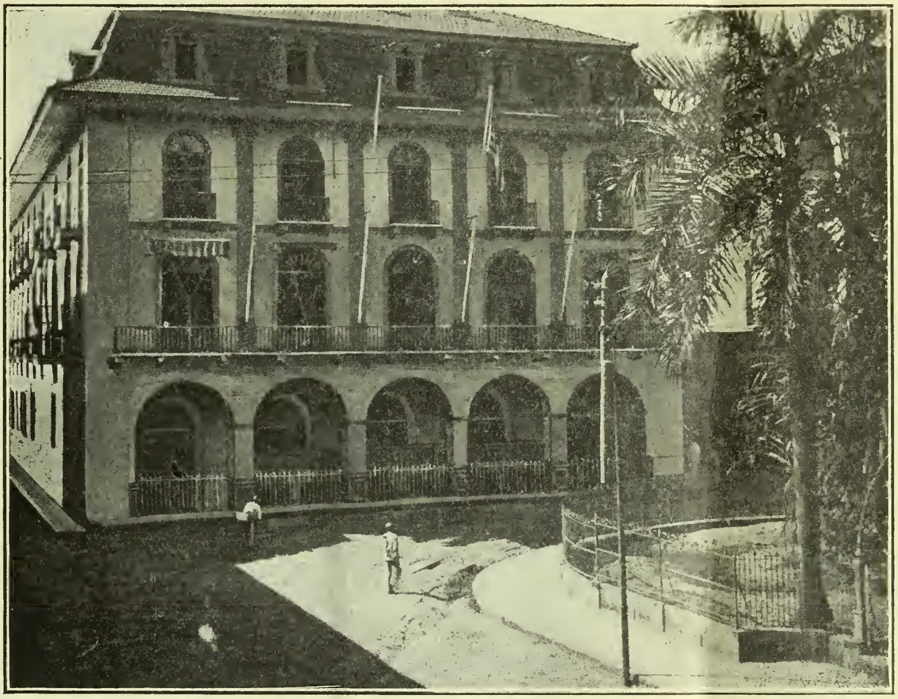
[2] Dr. Nelson: "Five Years at Panama."

We think four hundred years a rather long time, so long, in fact, it is almost impossible to realize that the French Canal Company spent in the years from 1881 to 1892 what was equivalent to considerably more than one dollar for every minute of time that has elapsed since Balboa first set foot upon the Isthmus of Panama.

During the early part of the nineteenth century the commercial prestige of Panama declined, but it was revived by the discovery of gold in California in 1849, the Isthmus being a part of the short route thither from the eastern United States. In consequence of this, and since the completion of the Panama Railroad in 1855 and the beginning of the canal work, the city has again become an important gateway of the Pacific.

We are inclined to think of the proposition to join the two oceans by means of a ship canal as essentially modern in conception, but there is said to be preserved in the town library of Nuremberg a globe made by John Schöner in 1520, only seven years after Balboa first saw the Pacific. "It is remarkable that the passage through the Isthmus of Darien (Panama), so much sought after in later times, is on the old globe carefully delineated."[3] According to the Encyclopedia Britannica, a proposal to build a canal across the Isthmus was also made in 1520 by Angel Saavedra. Nelson states that Gomera was the first among the Spaniards to advocate the union of the oceans by means of a canal,[4]



The Canal Building in Panama, in which are centered all the offices of the various departments engaged in the engineering and sanitary work of the commission.

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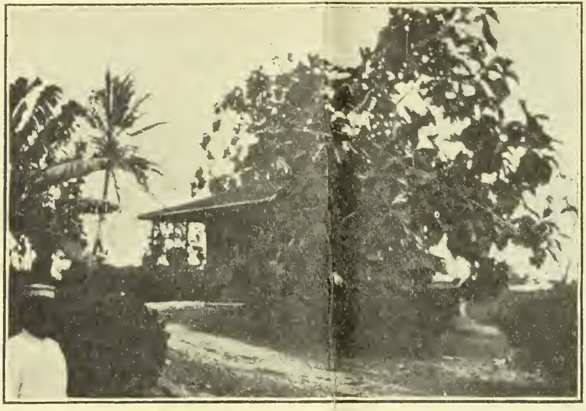
[3] King's Wonders of The World.

[4] Five Years at Panama.

and all the recent schemes—Panama, Nicaragua, and Tehuantepec—were submitted by him to Philip II. and his court over three hundred and fifty years ago. According to the same writer, the Dutch, Swedes, English, and Scotch have been prominent in the past in the consideration of the problem, and, as we know, the French and Americans in modern times. Humboldt revived the question in 1808, and new surveys have been made from time to time from 1824 until the present.



Large breadfruit tree on the grounds of the Ancon Hospital.

The rush of gold-seekers across the Isthmus on their way to California in 1849 made the construction of an interoceanic railway seem not only advisable but necessary. A survey for it was accordingly made, and ground was broken in 1850, the work being completed and the first train run from ocean to ocean in January, 1855, thanks to the high technical skill of the engineers, Messrs. Totten and Trautwine, who overcame almost incredible obstacles and difficulties. It cost in the neighborhood of $7,000,000 or $8,000,000, but has paid good dividends, since it carries and controls all freight from one ocean to the other, and since the steamship companies are said to have paid one-half of their total freight receipts to the railway company for the transit of forty-seven miles. The actual existence of the railroad in working order was one important factor in determining the undertaking of the canal by the French company, since, by its agency and aid, work could be begun and carried on at once at many points along the line.

Before considering the various concessions granted for the canal, it is worth noting that the Republic of Colombia, though it has several times changed its title and adopted new constitutions, claims to have maintained its integrity of territory from 1832 to 1903, when the new Republic of Panama declared its independence; that in 1846 a treaty was concluded between the Republic of Colombia and the United States whereby the latter guaranteed the neutrality of the Isthmus to the former and the sovereignty and property of the former; and that a new treaty between the two countries was ratified by the United States Senate in March, 1903, and was before the Colombian government for ratification during the following summer, but was rejected. This led to the revolution and declaration of independence by the former state, now the Republic of Panama, on November 3, 1903, the new republic being subsequently recognized by the United States.

View from the doctors' quarters at Ancon Hospital.

Several concessions for the building of the canal have been granted at different times by the Republic of Colombia, the first of these being to Baron de Tierry in 1835, the second in 1838 to other parties, and the third to Messrs. Cardenas and Gonzales in 1851. Three others followed previous to 1876, but work was not begun under any of them. In 1869 and 1870 it seemed probable that the United States would undertake the enterprise, as two treaties were actually signed by the Colombian government and the American minister, but the first of these failed to receive the support of the Colombian Congress, and the second that of our own Senate.

Finally, in 1876-7, a concession was granted to the Société Internationale du Canal Interoceanique, the chief movers in which seem to have been a General Türr and his brother-in-law, Lieut. Lucien Napoleon Bonaparte Wyse. Under the latter were made the first and second surveys for the present route, and he also devised plans for the construction of the canal and made an estimate as to the cost, both of these, however, proving subsequently to be entirely inadequate. In 1878 he had the concession extended to cover the entire Isthmus, and to continue the exclusive privileges of the canal to his company for ninety-nine years. Then, in 1879, the now celebrated International Congress was convened in Paris under the auspices of Ferdinand de Lesseps and with 135 delegates present. After sessions for two weeks it was decided that an Isthmian canal was feasible, that the route should be from Colon to Panama, and that it should be at sea level without locks. The meeting is said to have been thoroughly dominated by de Lesseps, and it is also asserted that it was he who had previously sent Lieutenant Wyse on his second expedition in 1878, when the extended concessions were obtained.

Pavilions of the hospital at Ancon.

Pavilions of the hospital at Ancon.

A new organization, styled the Compagnie Universelle du Canal Interoceanique de Panama, was formed, which promptly made de Lesseps its head and chief engineer, and also proceeded to purchase the concessions to the preceding company for the sum of $2,000,000. Next in order was a visit to the Isthmus by a technical commission made up of de Lesseps and numerous engineers, geologists, and others, which commission, after going over the route, adopted plans for a sea-level canal 29.5 feet in depth and with a bottom width of 72 feet, this requiring the excavation of 157,000,000 cubic yards of earth and rock. The commission's first estimate of the cost was $168,600,000, but de Lesseps subsequently reduced this to $127,000,000, and subscriptions were solicited on this basis with the promise of the completion of the canal in six years.

Actual work was begun in 1881, but it was soon found that as an engineer and surveyor Lieutenant Wyse was not all that the sound of his name would indicate, and that even de Lesseps had made his estimates far too low. Then came disease that slew the laborers by thousands, the subsidizing of the French press, bribery, graft, and deceit. As has been well said, it was a great financial debauch, involving the robbery of the poor and the corruption of those in high places. Exposure came in 1892, when the company was declared to be bankrupt, was dissolved by the courts, and a receiver appointed. Up to that time it had done only a small part of the work and had spent $260,000,000.

The receiver, having secured from the Colombian government an extension until 1910 for the completion of the work, was able to organize a new Panama company in the autumn of 1894 with a comparatively small capital of $13,000,000. This company then took over the assets and property of the old one and has been working steadily, though on a small scale, during the past ten years.

"An international technical commission composed of ten eminent engineers, representing the United States, Great Britain, Germany, and France, in November, 1899, reported unanimously in favor of the feasibility and practicability of completing the canal. They reported that the canal was already two-fifths completed, that not more than $102,400,000 would be needed to finish the work, and that the time need not exceed ten years."[5] Subsequent events have shown that these estimates were all probably too optimistic, as the same article in the Encyclopedia places the cost of finishing the canal at $184,000,000, this including the $40,000,000 paid the new Panama company by the United States, and as I understand that the present Canal Commission has estimated the excavation already done at forty million cubic yards as against ninety-four million yards still to be removed.

The esplanade on the old sea-wall at Panama, looking out upon the Bay.

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[5] International Encyclopedia.

The last stage in the history of the canal up to the present time begins with the law enacted by Congress in June, 1902, which authorized the President to purchase the property and concessions of the new company for $40,000,000, and with the acceptance in February, 1903, of the company's offer to make the sale for this price. Then followed the negotiations with the Colombian government for a new treaty, the failure of that government to ratify the treaty, the revolution of the State of Panama, its birth as a republic on November 3, 1903, and its prompt recognition by the United States. Of the treaty made by us with the new republic, of our purchase of the canal company's rights and property, of the establishment of the Canal Zone, and of the appointment of the Canal Commission of seven I need not speak, as these are doubtless all fresh in your memory.

We have at last reached a point where we may not only hope but may reasonably expect and demand that, under the auspices of the United States, the work will be carried on to completion speedily, honestly, and efficiently. Practically all of the future problems are now foreseen, and American skill and enterprise should solve each in its turn.

Need I say that of these problems the most imminent, the most persistent, and the most serious of all is that group of tropical diseases which exists throughout the Canal Zone, which has wrought so much evil in the past, which it is the province of this Society to investigate and study, and which, we believe, can be conquered by the science of modern medicine and sanitation? But all the measures now at our disposal, and all that we may learn in the near future by patient investigation and research, must be employed thoroughly and persistently if we would prevent the multitudinous deaths such as marked the era of the earlier operations.

Surely the Chief Sanitary Officer should be preëminent in his own domain. The conditions are such that he should and must have every facility and assistance that the resources of our government and our science can give, and he should not be hampered and hindered in his work by any bureaucratic regulations, however much these may be necessary or desirable in other departments of this enterprise. His task requires professional skill, executive ability, and individual judgment of the highest degree, for it is gigantic and will need every available resource at his command.

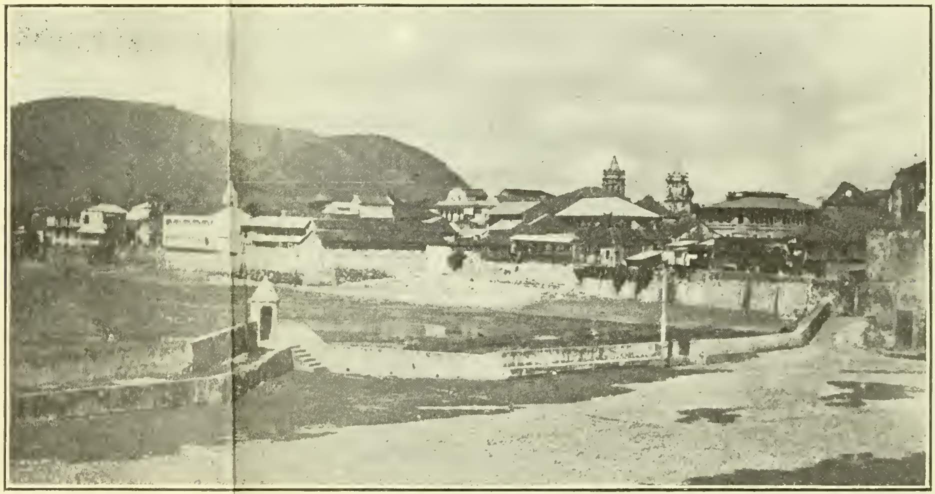
However, I believe that success can be achieved and that a great victory for Preventive Medicine can be won by representatives of our profession in this field. And I surmise that the American people, informed as many of them already are as to the causation of these diseases and the preventive measures that should be employed, will not bear it kindly if there is a repetition of the horrible death-tale of the past, especially if it can be traced to any interference with the work of the sanitary staff. I trust, therefore, that this Society will take some formal action that will call attention to and emphasize the preëminent importance of the work and duties of the medical officers employed in the construction of the canal, and that will help to secure to them every possible assistance for the successful completion of their labors.

Gatun and the Chagres River, seen from the Panama Railroad.

THE ISTHMIAN CANAL ZONE.[1]

BY JOSEPH MC FARLAND, M.D., PHILADELPHIA.

Those who approach the "Canal Zone" from the Atlantic side arrive at a port now known as Colon, in honor of Christopher Columbus, though until a comparatively recent time it was called Aspinwall. There is no real harbor at Colon, only a slight indentation of the shore line, and when storms arise, as not infrequently happens, vessels lying at the docks are obliged to run out to sea in order to save themselves from being dashed to pieces by the incoming waves.



The city of Panama, seen from the old sea-wall.

The first impression of the Isthmus when seen from the sea is pleasing, the land being mountainous, rugged, beautifully green. As the shore is approached palm trees and other tropical vegetation are gradually discerned. The town of Colon is picturesque when seen from the water, a long point of land with a row of cocoanut trees and a lighthouse being the chief attractive features. The town itself is somewhat scattered, and it seems to be along this strip of land, and especially on the side opposite the town, and away from the harbor, that the better residences are situated. But when one goes ashore it is to be greatly disappointed, for a more unattractive place can scarcely be pictured. The buildings are for the most part of wood, one and two, rarely three or four, stories in height, and mostly conveying an indescribable impression of neglect. The city is small, having only about three or four thousand inhabitants, chiefly negroes, who live in a state of squalor, surrounded by puddles of water and every kind of filth. Except the one street where the officers of the French Canal Company and a few well-to-do citizens erected their homes, there is nothing in the city of Colon at which one would care to direct a second glance. The surroundings of the city are low, marshy, and extremely unattractive. The Chagres River flows into the Atlantic Ocean not very far away, and the beginning of the canal excavation is distant from the city between half a mile and a mile, the city of Colon not being in the "Canal Zone."

The Panama Railroad, which connects the

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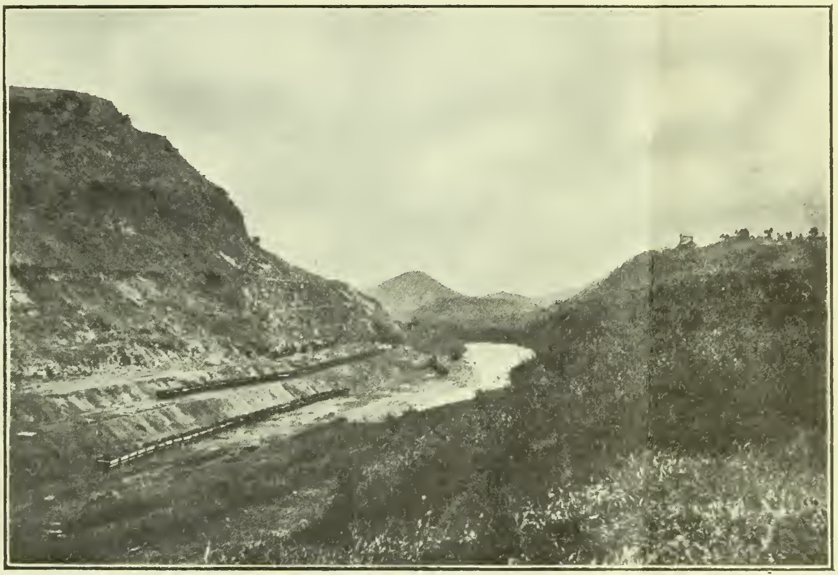
[1] Read before the American Society of Tropical Medicine, March 24, 1905.

Atlantic side with Panama on the Pacific side of the Isthmus, appears to be well constructed, and equipped with good engines and comfortable cars. It fairly well parallels the projected excavations of the canal, of which occasional glimpses are visible. As the train hurries on it traverses veritable tropical jungles. On each side are forests of large trees, between which a dense growth of young bananas, palms, and smaller plants is thickly interspersed, and upon which creeping plants of various kinds, with stalks varying from the size of the wrist to a delicate thread, have formed a dense fabric or hang in long, waving tendrils. One glance shows the impenetrability of these jungles without the aid of a machete or some other cutting implement. Now and then one sees a small banana plantation and a negro hut, or sometimes a group of such, or the train crosses a bridge and gives us a glimpse of a tributary of the Chagres River running between muddy banks, densely wooded.



The great canal excavation at Culebra.

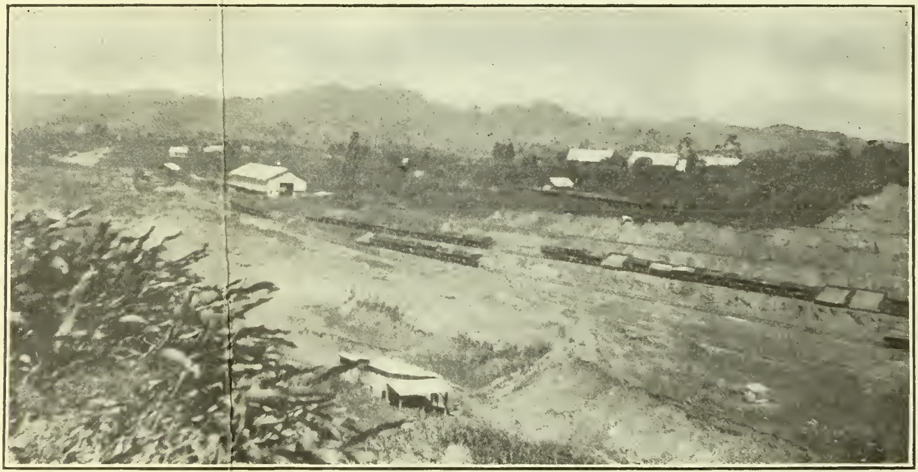
Not long after leaving Colon the little town of Gatun is reached, consisting of a small church, a few fairly pretentious buildings of wood, and a large number of thatched huts. This is on the steep bank of the Chagres River, which occasionally becomes so greatly swollen by the tropical rains as to rise twenty feet or more from its customary bed, and inundate the surrounding country. The railroad gradually ascends toward the center of the Isthmus, it being necessary to cross the mountain pass at Culebra, which is at the highest point. There are about two dozen small villages along the line of the Panama Railroad, each seeming to be less interesting than the others, as they are passed in succession. They usually contain a few shops, one or two saloons, called "canteens," a number of deserted barracks which formerly furnished habitations for the French employees, and a number of thatched huts occupied by negroes and Indian natives. The majority of the huts stand upon stilts to escape the dampness and tropical pests. One scarcely sees a white person, and, indeed, the fact that 90 per cent of the population of the Isthmus is made up of negroes amply explains this. As the higher ground is reached the marshy district is left behind, and precipitous hillsides, many laid out in small banana plantations, others overgrown with a dense mass of small trees, afford some variety to the scenery.

Empire is one of the most important stations on the road, and here one is obliged to change cars to see the principal excavation, that known as the great Culebra cut. Empire is a large town in consequence of its being a military post, and contains a number of canteens and shops. Otherwise there is very little difference in general appearance between it and a dozen others on the railroad. The military post of Empire is upon a hill, about three-fourths of a mile from the station, and at an elevation of several hundred feet. Four hundred United States marines are stationed here in well constructed barracks, the situation of which seems to be salubrious, as no death has occurred among them, and the amount of sickness has not been greater than in other military posts.

The view from the officers' "mess" is very pretty, the longest sweep of the canal excavation that can be seen at one time being visible from there, curving around the hill on the opposite side of the valley.

At Culebra when one finds himself standing on the edge of an excavation in the neighborhood of one hundred feet deep and one or two hundred yards wide, which can be followed for half a mile in each direction, he begins to understand the magnitude of the work of canal construction.

The only work in actual progress is done by two steam shovels, one French, the other American manufacture, recently introduced. The work thus far accomplished, all of which was done by the French, was intended for a canal to be built with locks. The amount of work necessitated by a sea-level canal will be greatly in excess of former estimates. We were shown a flag far up on the hillside which indicated the increased width of excavation necessary should the additional one hundred and sixty feet for the sea-level canal be undertaken, and it seemed almost incredible that the mountain side could be cut down in such manner. At the bottom of the cut there are some puddles of water left by the rain, and in them alligators are occasionally found.



The excavations at Culebra.

The ditches at Culebra contained trains of cars for the removal of the earth, numerous locomotives, and all kinds of excavating machinery, and near by there were shops, barracks, storehouses, and other buildings. We learned from Mr. Wallace, the chief engineer, that about 87 per cent of the machinery and apparatus left by the French were in serviceable condition, the metal parts having been carefully protected when the French abandoned the work. It was not, however, in use except in the Culebra district, where about 17 per cent of the available apparatus was actually being employed. He also said that it would probably be cheaper to introduce new modern machinery than to employ this antiquated apparatus, of which such a redundancy exists upon the Isthmus. It is difficult to estimate the amount of machinery that the French companies brought into and left behind them at the Isthmus of Panama. Upon sidings on the railroad one sees train after train of locomotives, small engines, hoisting engines, steamshovels, suspension apparatus, dumping cars, and many pieces the purpose of which was unknown to us, standing exactly where they had been placed years ago. It is said that there are enough sheet-metal dumping cars to form a train that would reach the whole forty-five miles across the Isthmus, but in addition to those we saw from the railroad, we were told that out in the jungles, entirely out of sight, are many similar trains of cars, etc., pushed out on sidings long since overgrown, and that in their recent surveying the engineers unexpectedly came upon train after train of cars and machinery. One reason for the disappearance of these trains is the rapidity with which the tropical vegetation grows. It is said that when a piece of land is completely cleared and then neglected, it takes but three years for the jungle to grow as completely as it was originally, with the exception of mahogany and other large trees, most of which have long since been removed from the district.

View of the canal excavation from the Officers' Mess at the Marine Barracks at Empire, showing the longest visible stretch of the canal.

From Culebra down the southern slope of the hills to Panama the aspect of the country changes. There is less water, hence the vegetation is not so dense, and bamboos and other plants that grow plentifully upon the other slope are absent. The hills are steeper, but less numerous, the towns more populous, and some of them more flourishing and better kept; and at last the train rounds the hill at Ancon and Panama is reached. Here begins the really delightful part of the trip, for Panama is a quaint old Spanish city whose stately churches, pretentious residences, and massive ruins tell of antiquity and historic vicissitude. The railway station is far from the center of civic activity, so that it is necessary to take carriages. The first part of the ride is over a dusty, unpaved road, crowded with vehicles and lined with dilapidated, uninviting habitations of the poorer classes. The city itself, however, has streets fairly well paved with stones, kept fairly clean, and in fairly good repair. The sidewalks are narrow and upon unequal levels, so that one occasionally has to ascend or descend one or two steps to walk upon them. The entrance to the houses is on a level with the sidewalk. The houses are two, rarely three and very rarely four, stories in height. They usually have several enormous windows on a level with the sidewalk. In the better houses these were closed, or securely screened, with ornamental ironwork, so that no one could enter from the street. Looking into the doorways one sometimes sees a central courtyard filled with exotic plants, but more often a dark, musty hallway, up which a stairway ascends. The majority of the houses have second-story verandas overhanging the sidewalk, and the roofs overhanging eaves so as to shade the verandas slightly. The better class of people delight to fill the verandas with plants and vines. In front of the principal churches there are open squares filled with handsome tropical trees, among which are numerous benches for the accommodation of the people, who are glad to use them as breathing places and playgrounds. The principal square or plaza is in front of the cathedral, and is surrounded by the principal buildings of the city. The church itself, with two square towers, is interesting, the stucco covering the towers being filled with mother-of-pearl shells. It is on one side, the old city hall and the so-called "Canal Building" on another, the principal hotel on the third, and the Bishop's palace on the fourth side of the plaza. Not far from this square the United States minister, Hon. John Barrett, has his residence, a large two-story edifice with immense rooms on the second floor, and two or three blocks away the palace of President Amador is situated upon the Bay. Beginning near the President's house a wide sea-wall, forming part of the old fortifications of the city, runs along the water front with a broad esplanade upon the top. This forms a favorite promenade in the evenings, and the bay beyond

The Marine Barracks at Empire.

is very pretty with its green islands and vessels riding at anchor. When the tide is out, however, one or two hundred yards of uncovered black rock and mud are exposed, and hundreds of buzzards circle in the air or alight upon the rocks in search of mussels or refuse. The air is always full of buzzards, though they do not light upon the houses in Panama so frequently as in Colon.

Cathedral at Panama.

The old city is in many ways very defective. Thus, for example, it has never had a municipal water-supply. It rains a good deal during eight months of the year, and the rain-water, caught in cisterns, is used for both drinking and washing purposes. When this supply gives out, water from various springs is peddled through the city in carts, and the best water sold in this way is brought in casks from a neighboring island. At the present time a municipal water-supply is provided for, and beautifully clear water will soon be piped from the neighboring mountains. There has never been any kind of drainage or sewerage system for the city. The rain washes the streets and collects in puddles in the lowlying districts, where it remains for a long time or escapes into the bay. Domestic drainage collects in cesspools. This, however, is being done away with at the present time, and the sanitary officials are engaged in completing a survey of the city for sewers, some of which have already been completed.

One of the disadvantages of not having a public water-supply and not having any drainage system was apparent in our hotel, where water was carried in buckets and poured into the bath tub, to be subsequently bailed out.

Until recently there was no municipal garbage collection or refuse removal of any kind in the place, rubbish being thrown into the streets, the dogs and buzzards disposing of it. But all this has been changed by the United States sanitary authorities under Colonel Gorgas and Dr. Carter, and at the present time one is impressed with the cleanliness and neatness of the city.

Yellow fever is endemic in the city of Panama, but it is hoped that it may soon be exterminated. The means to this end are (1) destruction of the breeding places of the mosquitoes by which it is distributed; (2) covering the cisterns with mosquito wire; (3) emptying, cleaning, and protecting the cesspools; and (4) by the judicious use of kerosene. Further, wherever a case of yellow fever occurs, the house is treated with pyrethrum vapor in order that the mosquitoes it contains may be destroyed, and the patient is at once removed in a mosquito-proof vehicle to a mosquito cage in the hospital at Ancon. There are, how-

The presidential palace, and home of President Amador, at Panama.

ever, several factors combining to make the extermination of yellow fever from Panama very difficult. Among these must be mentioned the considerable number of very badly qualified doctors in the city, who may not be able to recognize mild cases of the disease, and the frequency with which mild cases among the native children of the city go unrecognized and often untreated. From such cases mosquitoes constantly become infected, so that after all it is by the destruction of the mosquito, and by the protection of non-immune persons by mosquito nets and canopies, that most good will be done to prevent the spread of the disease.

A station on the Panama Railroad.

Malaria is more prevalent and much more dreaded than yellow fever, and indeed it is said that no one can remain two years in Panama without suffering from an attack.

One of the most interesting places from the medical standpoint is the canal hospital at Ancon. This was built by the French at the expenditure of several millions of dollars, though there is very little to show for the enormous amount of money expended. It occupies a steep hillside with an outlook toward the Bay of Panama. The hospital consists of a number of one-story pavilions, about which is a beautiful park of tropical trees and plants, with winding drives and walks, making the institution one of the most attractive spots in or near Panama. But the hospital, like the city itself, is not without serious defects, having no water-supply and no drainage system. At present, however, a reservoir is being built, and in a short time an abundance of pure, clean water will be available, while drains are being constructed to carry away the waste, so that the hospital will soon be as good in these particulars as others. But progress is extremely slow, and the lack of many things usually thought indispensable is most discouraging. Thus, for example, in a country where yellow fever and malaria are endemic, and where the prophylactic measures against them are chiefly directed toward the destruction of mosquitoes and the defense of the individual against their bites, we find the chief medical institution without adequate mosquito-wire defenses. It is true that there are canopies over the beds, and that yellow fever patients are kept in wire cages built around the bed, but the hospital pavilions are not screened. But it is surprising that so simple and inexpensive a prophylactic measure as the defense of all of the buildings by mosquito-wire should be omitted. It is equally disheartening that there is no laboratory, no laboratory apparatus, and not even a microscope belonging to the institution. These evils result from the distribution of authority, and from the niggardliness of commissioners unacquainted with the importance of the medical work to be done. There is probably nothing connected with the canal construction that equals in importance the prophylactic measures directed toward the prevention of such disastrous visitations of disease as we are told accompanied the activities of the French companies. Yet at the present time the sanitary department has no representative upon the Commission itself, is given no authority to go ahead on its own account, and is prohibited from incurring any expenditures without the approval of officers, who have it in their discretion to turn down any requisition regardless of its importance. One brings away the impression that the magnitude of the undertaking being beyond the capacity of the men appointed to do it, bad organization, improper distribution of authority, and petty jealousy have become the inevitable result. It is certainly to be hoped that our vigorous President will take matters into his own hands and effect a complete reorganization of the Commission, by which all of these evils can be overcome.

MEDICAL CONDITIONS OF THE ISTHMUS OF PANAMA, WITH OTHER NOTES.[1]

BY ROLAND G. CURTIN, M.D.

Dr. S. D. Risley, of Philadelphia, left with us, on the 25th of December, to attend the Fourth Pan-American Medical Congress, which was held at Panama. We went by rail to New Orleans, embarking there on the United Fruit Company's steamer *Beverly*. We passed down the Mississippi, across the Gulf of Mexico, through the Strait of Yucatan, and over the Caribbean Sea, arriving at Colon on Monday, January 2. There we were met by Senor Julio Icaza; the president of the Pan-American Congress, Pedro de O. Barrio, treasurer; John de Calvo, the secretary; and Dr. Perry, of the United States Marine Hospital Service, on duty there. In the afternoon we were taken over the Isthmus by the Panama Railroad. When we arrived at Panama City, Drs. Gorgas, Carter, and La Garde, and many public officials and citizens, met us and bade us welcome. We at once felt that we were among friends.

Colon was originally named Manzanilla. Later, at the time of the construction of the railroad, it was called Aspinwall, after the rich New Yorker that fathered the enterprise. The Spaniards, however, wanted a Spanish name; so it was changed to Colon. It is a town of over 5000 inhabitants. Although dirty, it is not so bad as it was six months ago. There is no underground drainage or pure water, the water that the people drink coming from cisterns connected with the roofs of the houses. These roofs are usually covered with vultures, birds not very unlike our Southern red-headed turkey-buzzard, but smaller. These birds cover the roofs with fecal matter, which is washed down into the cisterns, the water of which is used by the citizens. The cisterns, I was told, are cleaned out about once in every two years, when one or two inches of solid sediment is usually found and removed; but a successful business man of Colon informed me that his cistern had not been cleansed for ten years. He said, however, that the water was pure and contained no "wiggle-waggles" (meaning larvæ). I then suggested that the water might be too deadly to support life.

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[1] Read before the American Society of Tropical Medicine, March 24, 1905.

The climate of the Isthmus is typically tropical—damp, hot, and rainy. When we arrived we were told that the rainy season was over, and that it was then the dry season. It was not, however, so very dry, for I counted five showers on the first day after our arrival, and it rained every day that we were there. The rainy season lasts about eight or nine months. At Colon the rainfall is one-third greater than it is at Panama City—less than forty-eight miles distant. Another interesting difference between Colon and Panama is that the tide at Colon is about twenty-one inches; while at Panama City, on the Pacific, it is twenty-one feet. At the former place eighteen inches of rain fell last December, and one hundred and sixty inches during the year. Let us compare this with the rainfall of New Orleans, which is about twenty-seven inches, and with that of the city of Washington, D. C., which averages twenty-four and one-tenth inches. This great rainfall during the wet season is the cause of the marked and rapid rise of the Chagres River.

The temperature of the Isthmus ranges from 85° to 96° in the shade, the year around. Colon is said to be hotter than Panama City. The former place is only 522 miles north of the equator, and the Southern Cross is visible there in the early morning hours. The northeast trade-winds are almost constant; and, coming from the sea at Colon, they give its inhabitants more freedom from malaria and mosquitoes than on the Pacific coast. I was told that the Isthmus is occasionally visited by mild cold spells, called "northers," during which, with a cloudy sky, a damp northwest wind blows for two or three days. This is followed by a fall of temperature in the daytime from 97° to about 79°. This so-called coldness lasts for about one day. There are sometimes storms, and even cyclones, in the middle of the rainy season. I was informed that the rainy

The Panama Railroad. Most of the road is single track, a siding being shown in the illustration.

season is also the malarial season, but that the disease is not wholly confined to that season.

The population of Panama City is 20,262. The annual mortality is 52.71 per 1000, very little more than the death-rate of Havana when we took hold of Cuba. Now the death-rate of Havana has been reduced fully one-half. Ninety per cent of the population of the Isthmus are negroes, the other ten per cent being composed half of whites and half of Chinese and Indians. The native Indians and the Chinese suffer less from malaria than the people of other nations. In traveling over the Isthmus we noticed that the children looked remarkably strong and healthy. This we could easily see; for the half-grown boys and girls were, as the Rev. Dr. Palmore, of St. Louis, said, clothed only in their own complexions. It has been said that the devil is not so black as he is painted; and so, I think, it is with Panama's unhealthfulness. It is, I feel quite sure, not so bad as it has been reported to be. Other obnoxious tropical conditions I shall leave to those who have had experience with the disagreeable insects, so prevalent in tropical countries. Sightseeing during the day was in my case followed by skin irritation and scratching all night.

The sanitary problems are very much less intricate than were those at Havana, where Dr. Gorgas and his assistants so successfully labored; but we must remember that in Cuba there was a water-supply piped to the city at the time that we took hold of the problem. There was also an attempt at a sewerage system, although this was inadequate. In Panama the two cities have a small population, and are more easily managed on that account. When the necessary changes—such as a rigid quarantine, a proper water-supply, underground drainage, the removal of swamps and stagnant water, and the establishing of adequate hospital facilities—have been completed, the great menace to health at Panama will have been almost entirely annihilated. Much work in the way of draining the swamps and the ditches containing stagnant water that are found along the railroad and around the towns has already been accomplished. The filthy back yards have been cleaned; covered barrels for refuse have been furnished; cisterns have been covered; cesspools have been cleansed; and water that has been standing two days has been properly oiled, to prevent the propagation of the mosquito. We were all satisfied that the Sanitary Bureau is well managed and in most excellent hands. All that is wanted is to let them work without hindrance. Science will then assert

Laborers' barracks left by the French company.

itself, and Panama will be regenerated. Even after that, however, there will be danger from the extensive commerce with the West Indies and with South America, which will always be liable to introduce tropical diseases from the Atlantic and Pacific Oceans. This danger will be incurred later on, when the unacclimated population has been greatly increased, as it will be when the work on the canal is fully under way.

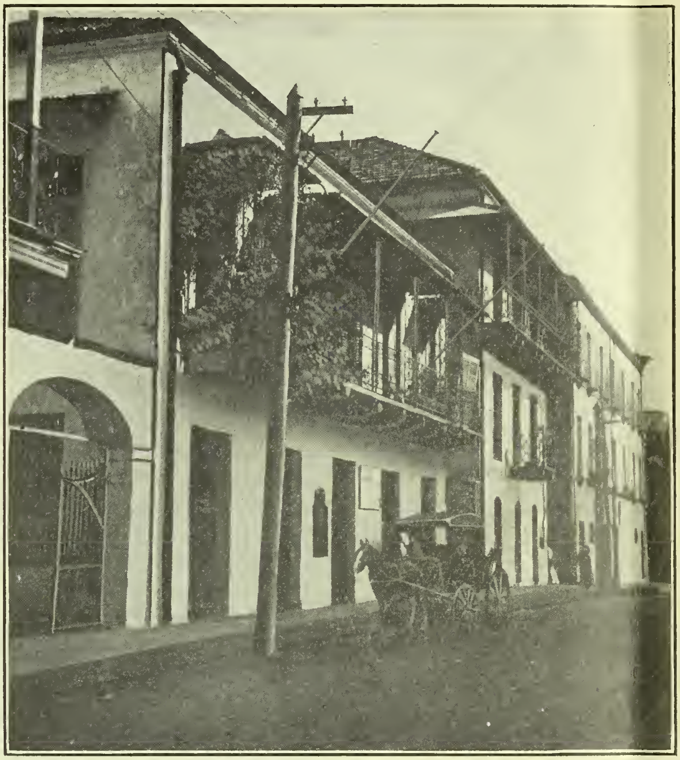
I had an opportunity while at Panama to talk with some of the intelligent residents upon the subject of the healthfulness of the country.

Typical street in Panama.

A Mr. Tracy Robinson, a native of New York, who has lived at Colon for the last forty years, told me that there had never been a marked epidemic of yellow fever on the Isthmus. This is probably owing to the fact that the population is composed almost entirely of immunes. He further stated that what he called the "cross-tie myth" (the story that during the building of the Panama Railroad a man had been buried for every cross-tie put down) means, when cut down to a truthful basis, merely that 1200 deaths out of a total of 6000 men employed in the construction of the road had occurred in persons that were unacclimated. This story has been persistently circulated all over the world ever since 1855, at which time the railroad was finished.

To show what tales are told now, even on the Isthmus, I may say that when we landed at Colon we were informed that there had been ten cases of yellow fever in that city, and that there were then twenty-four cases of that disease in the hospital at Panama City. I was assured by the medical officers in charge, however, that there had not been a case at Colon for months, and that there had been but ten cases in all at Panama City since we took charge of the Canal Zone. Among the homesick and frightened Americans that have lately gone to the Isthmus the wildest stories are circulated; and these are not only credited by them while there, but repeated after reaching the United States. The statistics of the United States marines stationed at Empire, on Culebra Hill, show that up to the time of our visit there had not been a single death from local diseases among the four hundred marines; and that the percentage of those in the hospital was not larger than would be found at the average post in this country. It must, however, be borne in mind that these soldiers live at one of the most salubrious spots on the whole Isthmus.

Yellow fever is treated on the Isthmus on the principle that it is produced only by the bite of the mosquito; although in the Congress there was a spirited debate as to whether it might not be contracted in other ways. The patients in Panama City are carried to the hospital at Ancon in wagons covered with mosquito-netting; and these wagons pass, on their way, within a few feet of the houses where the families of the doctors are sitting at the windows or out on the verandas. This shows that the medical staff have the courage of their conviction that the mosquito is the sole source of transmission. After the patient has been removed to the hospital the vacated room is fumigated with the smoke of a burned powder, consisting of a mixture of pyrethrum and sulphur. The patient upon reaching the hospital is immediately placed in a screened apartment. When Dr. Risley and I arrived at Colon on our way home, having just left Panama, our room was fumigated by the authorities.


One of the better residence streets in Panama.

Malaria is probably not more common on the Isthmus than it is in some localities in the United States; but in Panama it is an all-year-round disease. In his report for the month of November, 1904, Dr. Gorgas states that at Bohio the blood of 44 schoolchildren was examined, the malarial organism being found in 29 cases. Six grains of quinine a day was given to each of these 29 children for fourteen days, and their blood was then reëxamined. The blood of but five was then found to give a positive reaction.

Colon is near the mouth of the Chagres River, which, I am convinced, is not the deadly stream that it was once supposed to be. It is true that it is very malarious; but unacclimated persons that have for the last six months lived along its banks do not, as yet, seem to have been influenced by it. A supposed healthful outing for the citizens of Colon is to go to Gatun and float down in canoes to the mouth of the Chagres River, a distance of about seven miles.

In Dr. Gorgas's report of the 106 deaths that occurred in Panama City during the month of November, only 89 of which were attributable to the city, it is stated that the death-rate had decreased 19 from the month of October, 1904. I was surprised to read that beri-beri had caused ten deaths—the greatest number due to any one disease. Dr. Stern, of Panama City, informed me that this disease is always quite prevalent there, and is the cause of many, if not most, of the deaths. Nine deaths are recorded as having been caused by colic, eight by tuberculosis, eight by fever, and seven by bronchitis. Only one death is attributed to dysentery. President Amador, who is a physician, and Dr. Stern, who has practiced many years at Panama, both informed me that dysentery has never been what might be called epidemic, although it is usually present in Panama City and on the Isthmus. I heard of but one case of smallpox during my stay on the Isthmus, and this was taken from a ship at Colon while we were in that city.

Panama military police.

Colon and Panama City, the two largest places on the Isthmus, are not included in the Canal Zone, although located within the limits of the zone, which is ten miles wide. The United States has, however, control of both these cities so far as sanitary questions are concerned. Having visited the Canal Zone, it has occurred to us that, in the present condition of affairs, there are too many heads. This involves annoying and often serious delays, through the presence of too much "red tape."

I had an opportunity to talk with Chief Engineer Wallace in regard to the obstacles that must be overcome in constructing the canal. He told me that the most difficult problem is not the cutting away of the earth at Culebra cut, but the disposal of the excavated material. I suggested that this might be used to fill up the swamps along the Chagres River near Colon, which would undoubtedly add to the healthfulness of that region. He replied that this suggestion had been made before, but that to follow it out would be very expensive and would greatly delay the enterprise.

The newspapers are constantly referring to the difficult problem presented by the building of the canal along the Chagres River; but I was informed by Mr. Nichols, who is the engineer in charge at Gatun, that this problem is entirely imaginary. The river rises rapidly, sometimes several feet in an hour; and the railroad is sometimes forty feet under water. The floods usually occur in November; and Gatun, which is six miles from Colon, is the place where the river is in closest proximity to the canal.

Culebra is the highest point on the canal line between the two oceans. At its lowest elevation, where the canal will go through, it is about three hundred feet high. This is the most healthful part of the Isthmus. It is dry, well drained, and entirely free from swampy land.

Thatched huts of the natives of Panama. A large part of the rural population lives in such habitations.

In traveling over the Panama Railroad I

noticed that the telegraph-poles were made of wrought iron. I was told that wooden ones had been used at first; but that, being cut off below the surface of the ground by the boring-worms, these poles had soon fallen. Small arches of stone were next erected, the stones being fastened together with cement. On the top of each arch was placed an elongated pyramid, composed of small stones connected together in the same way; and on these structures the wires were placed. Scarcely had these arches been put up along the line of the railroad when an earthquake caused their sudden downfall. I was told that only about three are still standing. One of these I had an opportunity to see, and at first took it to be a wayside shrine. After these experiences iron poles were erected, and with these there has been no trouble.

I was much struck with the small amount of animal life seen on the Isthmus. There are very few birds, the most of which have bright plumage, but seem to have no song. In the Caribbean Sea I noticed very little marine life. The flowers, also, while beautiful to look at, have no fragrance. All this was very disappointing.

Before leaving the Isthmus a Panama breakfast was given us at Taboga Island, in Panama Bay, a part of the Pacific Ocean. President Amador and his charming wife accompanied the party. This island, which is ten miles from Panama, is twelve miles in circumference. Its sides are abrupt, rising at one place to a height of one thousand feet. It is a veritable garden spot, where are grown pineapples, bananas, and cocoanuts, said to be the best to be found in the world. It possesses many mineral springs of iron and magnesium. I was informed that the inhabitants of the island lose their teeth early, owing to the iron. This seems to indicate that the water is markedly acid.

The island has a population of twelve hundred, twenty-four of whom are lepers, and the rest largely fruit-growers and cottagers. It is far enough away from the lowlands of the coast to be free from mosquitoes and other swamp influences. Having an ocean, rather than a seaside, climate, it forms a convenient place for malarial cases and hospital convalescents to recuperate. Malarial patients are quickly cured by a sojourn there; and persons with lung diseases are sent there from the whole Isthmus—in many cases with benefit. It is the health resort of the Isthmus.

The National Panamanian Band, playing their own national airs and those of the United States, was always in evidence. These musicians followed us to Taboga Island, to Culebra, to Sabanna, to the ball, the banquet, and to every place we were invited to go; and a midnight serenade was added to the festivities of the occasion. The Congress and the band reminded me of Mary and her little lamb:

Part of the barracks at Empire.

Everywhere that Congress went
The band was sure to go.

I felt lost when we parted company.

In closing, allow me to say that we were most hospitably entertained, receiving during our stay on the Isthmus nothing but kindness and courtesy at the hands of the United States sanitary officials, the Panamanian government, the medical practitioners, and the citizens generally.

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The American Society of Tropical Medicine.

1907.

The American Society of Tropical Medicine.

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Reprinted from the New York Medical Journal for July 7, 1906.

FIGHTING PLAGUE IN JAPAN.*

By Professor Shibasaburo Kitasato,
Tokyo, Japan,
Director of the Institute for Infectious Diseases, Tokyo.

Published under the imprimatur of the American Society of Tropical Medicine, March 21, 1906.

Plague Epidemic and Its Detrimental Effects.—An epidemic of plague such as had formerly raged in India and Hong-Kong was introduced into Formosa in 1896, since when that island has become a permanent seat of dangerous plague. Since Japan came into possession of this island, it has become almost impossible for her to get rid of this fatal disease. However, a strict enforcement of the preventive measures and quarantine systems has produced a good effect in preventing its intrusion into the mother country. But the danger soon began to present itself from quite other sources. when in 1896 the first case of plague was found on board a vessel that had just entered Yokohoma. She brought the dangerous germ from India and Southern China, with which regions Japan now has frequent commercial intercourse. Since this event, steamers arriving at Yokohama, Kobé, and Nagasaki have brought several cases of bubonic plague, but the discovery having been made in due time and preventive measures and quarantine properly applied, the infection was avoided, for a time at least.

It seemed to be not the patients, but inanimate objects that introduced the plague. Vessels coming from infected regions, such as Bombay and

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* Written for the annual meeting of the American Society of Tropical Medicine, March 21, 1906.

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Hong-Kong, began to introduce into our country the plague germs, which happened to be mingled with their freight, principally consisting of cotton. Unaware of the fatal germs, we allowed the freight to be landed, with the consequence that the infection spread rapidly in the principal trading ports. The epidemic prevailed first among the rats and then spread among men, with the result that many human lives were sacrified, and tens of thousands of yen were expended in fruitless attempt to stay the disease. The foreign trade of the country also suffered considerably.

The principal epidemics in Japan have been as follows: The first outbreak of plague was during the year 1899-1900. It began in Kobé, and then spread to Osaka, where the ravages reached a high mark, and went as far as Hamamatsu and Wakayama. The total cases during this epidemic numbered 230.

The second one was during the year 1902-1903. The source of this outbreak was probably the cotton imported from Hong-Kong. The first case was discovered in Yokohama, and the infection spread to a restricted portion of the city of Tokyo. The epidemic was successfully combated with the combined efforts of the two cities, after it had claimed seventy-one victims.

The third one is that of 1905, which is still prevailing. It has already claimed a number of poor victims in several localities, namely, Tokyo, Chiba, Kobé, Osaka, Kagawa, and Moji. The epidemic of Tokyo broke out in the early spring of the year at Fukagawa, and then spread to Chiba, where we experienced a slight case of summer epidemic. From May to the middle of June the plague raged in a village of the Kagawa prefecture and spread among the fishermen by direct contagion. In its severity this epidemic is unparalleled in recent years. It appears to have been caused from an origin similar to that of the epidemic in Osaka and Kobé, as stated below. In August two patients were found in the city of Kobé, and within a few months the number increased rapidly so that during the last year (1905) the total number of the victims amounted to ninety. Next to Kobé, Osaka suffered the most, having had a large number of patients—134 in three months—since October last. In both cities the epidemic spread over the whole area and is still raging. The germ was carried to Moji, where it claimed nine victims. The plague was unprecedented both in severity and in the number of victims, the total cases during the last year having reached to 297.

The number of the patients during the last year in different localities has been as follows: Tokyo, 15; Chiba, 11; Osaka, 134; Nara, 2; Kagawa, 36; Kobé, 90; Moji, 9; total, 297.

The following table shows the regions and numbers in the series of outbreaks in Japan:

Year.	Patients.	Deaths.	Principal region of epidemics.
1899	62	45	Kobé, Osaka.
1900	168	153	Kobé, Osaka, Hamamatsu, Wakayama, Nagasaki.
1901	2	2	Wakayama.
1902	14	9	Yokohama and Tokyo.
1903	57	49	Yokohama and Tokyo.
1904	1	1	Kobé.
1905	297	257	Tokyo, Kobé, Osaka, Chiba, Kagawa, Moji, Nara.
Totals..	601	513	

The money spent for preventive purposes and quarantine reached an enormous amount. During the first attack Osaka city spent more than 352,500 yen;[1] during the second outbreak Tokyo city, although her patients numbered only fifteen, spent 220,000 yen; i. e., 14,600 yen for each victim. The figures only show how expensive an outbreak of plague is, to say nothing of the dreadful effects upon human life. From the above mentioned facts, it may easily be supposed how great a burden the present epidemic which is raging in Kobé and Osaka with unparalleled vigor will bring upon the financial resources of the country. The city of Kobé spent 310,000 yen and Osaka spent 470,000 yen for preventive measures; and it is clear from the present condition that we shall have to spend a far greater amount to keep the plague at bay.

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[1] A yen is equal to about one dollar.

These are the direct burdens imposed upon the finances of the country, but this is not all; for the indirect detrimental effects should be also considered. The loss is inestimable, because it is such a wide and far reaching one, affecting both domestic and foreign traffic, that it cannot be compared with any other kind of epidemics, even without considering its direct damages upon a limited community. Plague is indeed the most fearful enemy of mankind.

From our studies of epidemics in Japan we can see that there are two ways in which it might be introduced. The one is by contagion from plague patients imported and the other by contact with the disease germ mingled in the freight brought in from some infected regions. Preventive measures depend upon these ways. If the way be by plague patients discovery is made easier, and the preventives or quarantine, as the case may be, can be applied promptly so that the ravage can be confined within at least a small radius. On the other hand, if the disease germ is going to be propagated through the medium of the rat tribe, prevention becomes more difficult; for at the same time that the discovery of the infected rats is made human beings are already the victims. Moreover, at the moment that man receives contagion from rats the ravage of epidemic as a rule reaches a high mark, so that the outbreak soon assumes a character difficult to control, and the ravage spread far and wide, affecting both men and animals. Such a case may be illustrated by the first outbreak and by the present epidemic, in which Osaka and Kobé are the chief sufferers. The ravages at Chiba and Kagawa may be taken as an example of a case in which the source of the epidemic was a human patient. In this outbreak we were able to have the ravage confined within a small locality by promptly applying the preventives, that is to say, before the rat tribe was attacked by the germ. We can see thus the same preventive measures giving different results in different cases.

In every case of epidemic it is difficult to ascertain the exact circumstances under which plague is introduced. This is especially so when the medium of propagation is something other than a human patient, notably rats. So far the plague epidemics in Japan have in every case been first discovered in localities communicating directly with foreign countries and have then spread to internal regions. Moreover, the first case in a locality that has subsequently become the source of the epidemic has been invariably associated with freight imported from infected regions. The first epidemic broke out from a steamer that entered the port of Kobé, bringing in raw cotton and Chinese rice from Bombay and Hong-Kong. The second epidemic may be traced to a vessel that entered the port of Yokohama with a freight consisting of raw cotton. The present epidemic prevalent in Osaka and Kobé may be traced to a vessel in Kobé harbor, on which the raw cotton was imported from Bombay to the Cotton Spinning Company in Kobé. These show almost identical origins for the fatal pestilence.

As a rule, the plague germ on entering these trade ports does not directly attack men; it first infects the rat tribe, and by the time human victims have been discovered the disease has assumed a well advanced form. This fact has been seen in several occasions. The present epidemic in Osaka is a case in point. It was preceded by the discovery of infected rats in February, and during May of the same year human victims began to appear, thus showing how deep rooted is the source of infection.

With respect to the season it has become evident that a winter epidemic is generally of a chronic character and rages for a long period, spreading over a large area. The severity of the disease is also shown by an epidemic of this nature. To this class belong the first and the present epidemics in Osaka and Kobé, and the epidemic which occurred in Tokio and Yokohama. A summer epidemic is usually acute in character and spreads as a rule by contagion. It is severe, but is of short duration, and is limited to a small area. To this class belong the epidemics in Chiba and Kagawa last year, and that in Hamamatsu in 1900. It is noticeable that during a winter epidemic a large number of rats are found infected, whilst in a summer epidemic infected rats are rarely if ever found.

Preventive Measures.—It has been shown that plague epidemics in Japan have their origin in the regions of the Indian Peninsula, South China, and Formosa. The first and most urgent step in the way of preventives is therefore to put the vessels coming in from these regions in quarantine. Hence, quarantine stations have been erected at Yokohama, Kobé, Nagasaki, Moji, and other principal trade ports, and quarantine measures enforced as strictly as possible. Plague infected vessels are forbidden all communication with the land, and are to apply the rat killing measures and other sanitary methods. For killing rats aboard a vessel, specially constructed rat destroying boats, similar to those used in the port of Hamburg, Germany, are to be despatched. These boats are provided at Yokohama, Kobé, and Moji, and are now in use.

To the bureau of public health under the Department of the Interior belongs a special office for adopting and executing measures against infectious diseases. Its officials are composed of physicians and surgeons, their assistants and quarantine commissioners. Each municipality or prefecture has also instituted a board of health, consisting of one physician and several assistants with a number of inspectors. This organization is placed under the direct control of the police department. They take charge of all the matters relating to infectious diseases. The principal prefectures and districts are provided with isolating hospitals and laboratories to receive

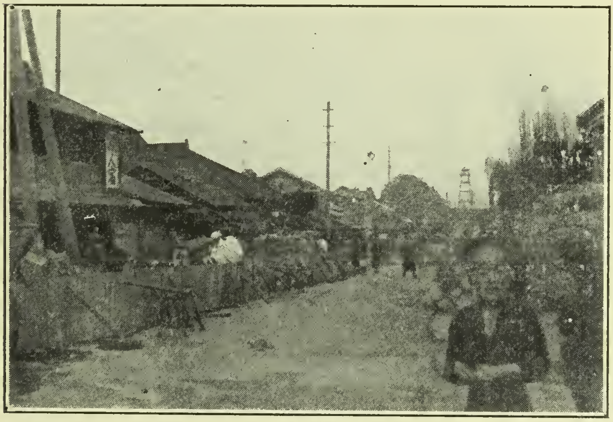

FIG. 1.—Disinfection of the infected houses, showing how to inclose the area with a zinc wall.

patients, and to take necessary preventive measures. In cases of plague outbreak the prefectural governments increase the number of officials so as to meet the occasion. When an outbreak is of unusual vigor an imperial ordinance is issued by which is ordered the organization of a special board for preventives against plague, consisting of commissioners, inspectors, clerks, and watchmen. Several councillors are also to be appointed whose function it is to submit advice on the matters in question. On account of the present outbreak Osaka municipality has in commission 311 officials and several councillors.

In Japan all affairs relating to health and sanitary measures, particularly to the preventive measures against infectious diseases, belong to local administration; but the execution has to be carried out with the aid of the police. The expenses required for the purpose are borne by the people of the locality with the aid of financial resources of the prefectural or municipal government. The central government, moreover, has promised to aid the local governments in case of an outbreak of contagious diseases to an amount not exceeding one sixth of the total expense. In case of plague, however, the central government has spent and is spending an enormous amount far above the fixed rate.

The Institute for Infectious Diseases acts as councillor to the government for matters relating to health, and especially to the preventive and sanitary measures against infectious diseases. In time of plague epidemic the institute furnishes, through governmental appointment, those commissioners and officials who take charge of preventive and sanitary measures. It has a plague laboratory conducted by the most advanced scientific methods. Here are prepared pest serum and vaccine for the use of the whole country. As a part of its work it gathers a number of physicians and surgeons from all parts of the country, and gives a course on bacteriology and epidemiology. Those who have already finished the course in the institute number at present 1,293, and may be found scattered throughout the country. At least, a part of them is now actually engaged in important work in hygiene and preventive affairs.

As these specially educated physicians and surgeons are located throughout the country, it is an easy matter to gather several hundreds of commissioners at once in a time of emergency. To fight the plague there is usually needed a large number of experienced physicians; and for this preparedness the country owes much to the institute.

Such is a brief account of the organ for the preventive work done in Japan. I must here express my sincere admiration at the way in which the United States is providing against infectious diseases by appointing medical officers to be stationed at the principal ports of the world. I believe that preventive measures against plague are the most urgent need of the age, but in order to be of permanent good the measures should not only include the temporary suspension of the intrusion enforced at one's own ports, but medical officers should be stationed at the infectious source, where departing vessels should be strictly examined. I have suggested that officials should be stationed at least in ports of India and South China, to which the plague outbreaks in Japan had been traced.

In fighting plague, quarantine on ports, however strict and complete, cannot be solely relied on, hence the general measures of providing against the infectious diseases throughout the country must be perfected. As plague cannot be considered among ordinary infectious diseases, the regulation bearing on the infectious diseases in Japan were found unavailable, and the government had to remodel them so as to meet with the needs of the time. The principal features in the new regulations may be stated here:

1. Disinfection; discommunication; isolation; the preventive measures against infectious diseases to be enforced not only upon patients, whether dead or alive, their houses and furniture, but upon all suspicious cases.

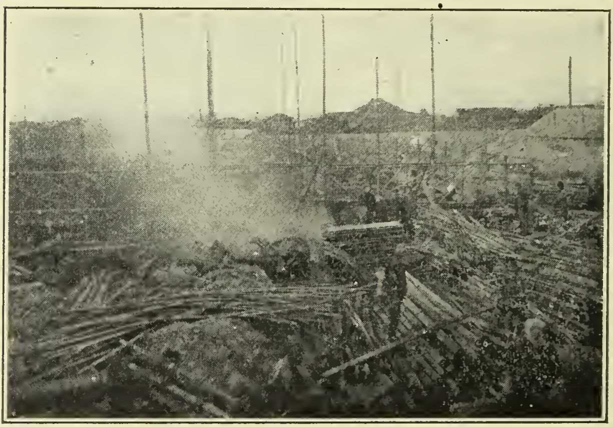

FIG. 2.—Disinfecting the cotton.

2. For disinfection of plague all rats must be killed.
3. If infectious patients are found suffering from plague, the days of isolation should not be less than ten.

These regulations were based on the experience of several years. As to the disinfection it is necessary to make its area as extensive as possible, as the plague germ is very easily propagated. Again, bubonic plague often develops pulmonary or dermic plague, and the disease not unfrequently infects by direct contagion, especially in time of epidemic; discommunication and isolation, therefore, must be strictly enforced. A fixed isolating period of ten days was desired as the incubation period of the plague lasts from six to seven days. Killing all rats if possible was deemed necessary from the fact that the animal has the closest connection with plague. These principles were applied where the intrusion of the pestilence was suspected previous to the formulation of the new regulations.

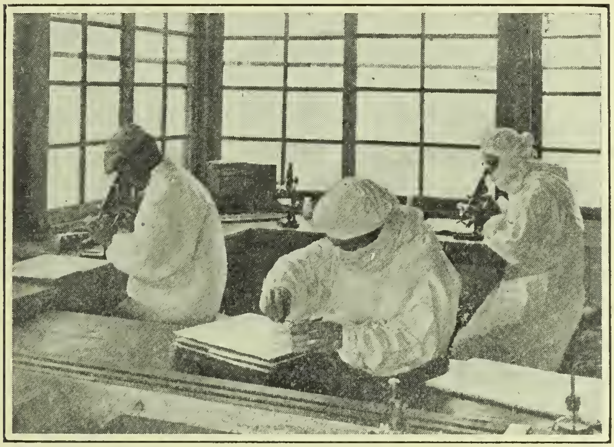

FIG. 3.—Laboratory work.

In killing rats it is important to remember that traps and appliances should be set in all buildings, particularly those which contain cotton and grains in which the plague germ is most liable to be stored. I gave out a warning in this respect and made a suggestion a few years ago, as the result of which the municipal government of Tokyo issued an ordinance respecting building of warehouses. According to this ordinance all buildings must be constructed so as not to allow a place of abode for the rat tribe. Similar regulations have been adopted in other cities and prefectures, especially in places directly connected with foreign countries. Legal acts appear rather despotic; nevertheless, it must be regarded a necessity in view of the dreadful character of the disease that is propagated by rats. I believe that the application of such a rule should be permanent not only on warehouses, but on all dwellings, making them all "rat proof," then the danger of infection would be greatly lessened. Such a step is yet to be taken.

Sanitary Works.—The principal works realized from the preventive measures are: 1, Bacteriological examination; 2, searching for patients; 3, killing rats, disinfection, and application of sanitary methods; 4, disposal of patients and of infected articles. The work may be briefly described as follows:

The bacteriological laboratories in different districts and prefectures, which in ordinary times are used for examination of infectious diseases in general, have been specially provided with facilities for the study and examination of plague, and in the time of plague epidemic they may be used for this special purpose. In such places as Kobé, Osaka, Yokohama, and Tokyo, which are most frequently threatened with plague intrusion, the government has been encouraging the destruction of rats for several years past by buying from the people all rats killed or caught. This practice has a twofold purpose, one the preventive of an epidemic, and the other to ascertain if there be found any infected rats, as these usually precede an epidemic among men. Each of the rats bought by the government, immensely numerous in number, is examined bacteriologically. In the laboratory of the board rats from 3,000 to 4,000 in number are daily examined, even in ordinary times, and in time of an epidemic the number reaches an enormous figure. As the plague outbreaks in Japan are usually preceded by the infection of the rat tribe, the examination of rats may be regarded as a sort of reconnoitering work. The use of the reconnoissance may be illustrated by the fact of the infected rats having been discovered in Yokohama in 1902 before any human victim could be found, and the warning was given in time. Examining rats was even more necessary in time of an epidemic, for it was only by such processes that the conditions and manner of propagation of the plague could be actually known.

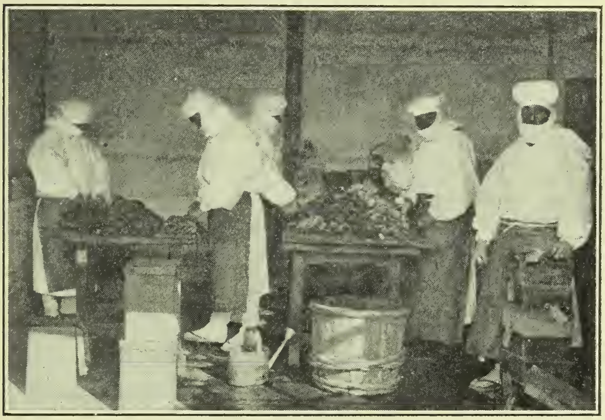

FIG. 4.—Examination of rats.

From the experiences of the past it may be suggested that in examining rats particular attention be paid to the submaxillary, and cervical glands, and spleen of the animal. Those organs in most cases show the evidences of infection if there be any. The inference drawn is that the rat tribe receives the plague germ through the mucous membranes of the mouth and throat. An important work during an epidemic prevalence is the bacteriological examination of the matters obtained from the patient or the dead, for the diagnosis of plague depends on both clinical and bacteriological examination. In suspicious cases materials for examination are taken from the affected parts, such as glands or skin lesions, and the expectoration of the patients is frequently subjected to examination. In the dead, the heart blood, spleen juice, and the contents of the glands or lungs are to be examined. In connection with these materials, microscopical examination, germ culture. and animal experiments are carried on. Agglutination for the pest serum is also unavoidable. It is, of course, difficult by any of these methods to ensure the discovery of infection, but many cases are on record in which suspicious things, such as cotton filth and decayed grains, were really found infected with plague germ. Such a case was illustrated in Osaka in 1899 when cotton filth revealed plague germ under bacteriological examination.

Searching for the patients is also an important work of prevention, especially when intrusion of plague is suspected. Physicians are generally expected by law to report when an infectious disease is discovered, but such reports are in most cases unavailable, for they cannot be relied on regularly. During an epidemic period the number of plague cases brought to light by physicians' reports amounts to only one tenth of the whole number of patients actually existing. So far, the physicians in the localities where plague never was seen before have been ignorant of the disease and have permitted the epidemic to spread rapidly. This unfortunate fact was illustrated by the outbreak in Kagawa last year. As a means of promptly seeking out the patients in places which are frequently menaced with the intrusion, the physicians attached to the police are intrusted with the power of examining the dead from acute febrile diseases. That such examination should not be neglected has been shown by our experiences during epidemic periods, for it has given the same result as the reconnoitering work by the examination of rats. The following shows the finding of plague patients during the present epidemic in Osaka and Kobé last year:

	Osaka.	Kobe.
Physicians' reports	49	30
Inspection of dead	27	26
Inspection from house to house	34	33
Isolation	17	0
Miscellaneous	4	1
Totals	131	90

From the foregoing table it will readily be seen that if the dead had not been examined, twenty-seven cases in Osaka and twenty-six cases in Kobé which were found to be really infected with plague would have been regarded as cases of ordinary diseases, thus increasing the sources of the epidemic. It must be admitted that it is not an easy task, though a very necessary step, to inspect apparently healthy persons living in an infected locality or its vicinity. The districts where the epidemic is most liable to prevail are the places where ignorant people reside, and this fact hinders the progress of the health inspecting officials. Only by their devotion to duty and work could these physicians succeed in their efforts. Their admirable work was illustrated during the outbreak at Tokyo in 1903, where in every case, except the three early cases out of the total of thirteen plague patients, diagnosis of apparently healthy persons gave a warning hint, and the patients were promptly removed and isolated. In the present epidemic in Osaka and Kobé not a few dangerous cases were discovered by the inspection of persons, as the foregoing table shows. The task of finding plague cases by such methods, however, becomes difficult in proportion as the epidemic spreads further, and the patients are found scattered over a wide area.

Plague in a patient or a dead person has to be ascertained, as stated, by both clinical and bacteriological examinations, but application of such a test needs to be done as speedily as circumstances permit. The determination of a plague case was usually effected within forty-eight hours after the finding out of the suspicious patient or death. During the examinations the patient or the dead person is to be restricted as though a real plague case.

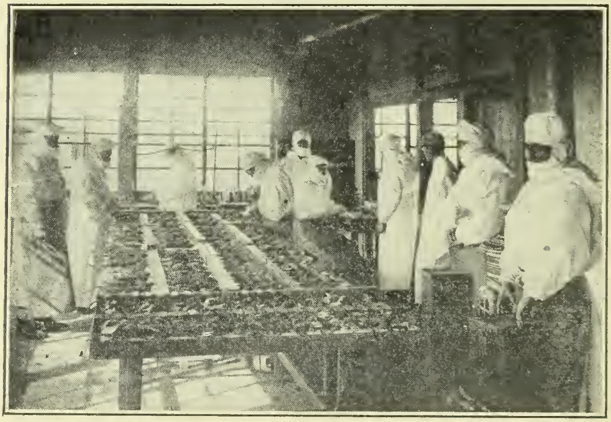

FIG. 5.— Examination of rats.

In localities where imported freight is stored, or laborers live, or of imperfect sanitary surroundings, rat killing measures are enforced even on ordinary days. In time of impending intrusion of plague rat killing measures are generally enforced. Two days at least previous to the application of sanitary system rat killing devices, traps, and poisons are provided for every dwelling and warehouses. In buildings that can be tightly enclosed, vapor of formaldehyde or sulphurous gas is set free. All such places as permit abode to rats are to be rebuilt, sewerages to be improved, and filth burnt. These constitute the rat killing sanitary measures. Occupants of the dwelling where plague patients are found, or where infected rats are frequently found, are to be removed and the whole building disinfected by the application of the rat killing sanitary measures. Around such buildings are constructed zinc walls, and in the neighboring sewers are set metal nets. If the infected place includes an extensive area it is divided into small sections, and a similar method is applied to each section. The first step in sanitary method is to disinfect the furniture, search for rats, and then disinfect the whole building. As disinfectants carbolic acid, sublimate, and lime water are used. Articles of a suspicious nature are sometimes steamed, boiled, or burnt. The disinfected objects are then exposed to the sun.

In applying disinfection in some instances it is desirable to destroy the whole building by fire. I believe we should be justified in taking such extreme measures as a means of absolute disinfection, in case the infection has not yet spread to a wide area and for a building situated in such a position as to inconvenience the application of sanitary measures. Such a measure was not infrequently taken in Japan. Before setting fire to a building precautions are necessary to prevent rats from escaping to neighboring houses to which they might carry the germ. This is done by surrounding the house with zinc walls.

Difficulties of disinfection by absolute destruction of the whole house are in many cases unsurmountable. This is particularly so when plague patients and infected rats are found scattered over a large area. The present epidemic in Osaka and Kobé illustrates such a situation, as in these cities the ravage is not confined in a small area, but scattered throughout the whole of the cities. Had extreme measures been applied in these cities the whole districts would have been burnt.

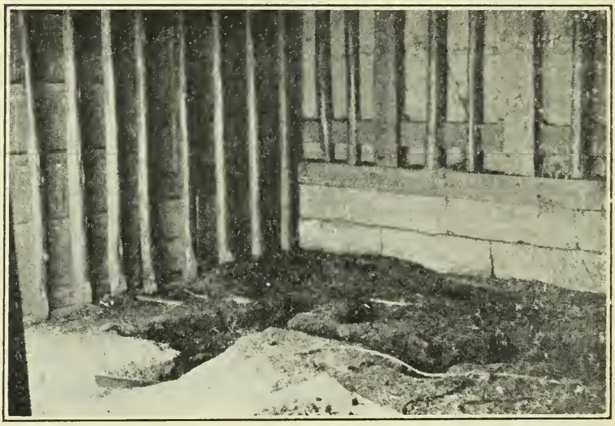

Fig. 6.—Searching for rats in a warehouse.

The zinc walls used in connection with the disinfection display a peculiar appearance. They serve to keep off the rats from infected places. The effectiveness of walling in a small area before epidemic becomes vigorous has been illustrated during the outbreak in Yokohama and

Tokyo. The height of the walls varies according to different circumstances, but usually it is of about three feet from the ground with a foot or two buried in the earth, so that rats can neither climb over such a wall nor go under it. The use of zinc for such a purpose is apparent, for it is not liable to rust like some other metals, and may be used repeatedly. These zinc walls were built in every epidemic period, but the largest of them were those built in 1903 in Tokyo. These walls inclosed an area of about three quarter square mile, with partitions dividing it into several sections. Besides, every place where infected rats were found was inclosed with a wall. The total length of the zinc walls measured 204,148 feet, or about four miles.

The discovery of a plague suspected patient is to be promptly followed by the proper measures to prevent further spread. Inspecting physicians hurry to the patient's residence, and if the suspected person proves to be a real case, he is at once conveyed to a hospital for infectious diseases, or to an isolating hospital where proper treatment is given. Should the discovery be made in a dead body, the remains are first disinfected and then disposed of by cremation. Each member of the infected family, and suspected persons in the neighborhood, are sent to an isolating house. Even apparently healthy persons are subjected to daily examination during the days set for isolation. They are treated with all the possible means of disinfection and prevention, including the inoculation of the pest serum, which gives passive immunity. Those who are in less danger are inoculated with the pest vaccine.

The pest serum and vaccine have been used in every epidemic, those who were treated with the remedies numbering tens of thousand. We have been unable to obtain the exact statistics during the epidemic periods in the main Japanese islands as to the value of these remedies, and the question remains yet to be settled definitely as to the susceptibility to the infectious influence of those who have received the administration.

In the outbreak in Tainan, Formosa, which occurred in 1901, the conditions enabled us to obtain a valuable set of statistics, and the enormous number of persons who were vaccinated gave hints as to the value of the vaccine. Of 10,876 inoculated persons in Tainan only seven were attacked by plague; while out of about 40,000 persons who failed to receive the treatment more than five hundred were infected with the disease. From such facts it is not difficult to believe in the favorable results of the vaccination, although we are not yet in a position to assert its value conclusively.

Those plague commissioners and officials who at the call of their duty have to come in contact with the dangerous patients have received the inoculation of the serum. During every epidemic officials have been inoculated with the small quantity of the serum (sixteen to twenty c.c.) and none of them has yet been infected. During the present epidemic in Osaka and Kobé prophylactic serum inoculation was applied to the persons who were members of an infected house. The results of the prophylaxis are as follows:

TABLE SHOWING THE NUMBER OF PATIENTS.

	Osaka.	Kobé.	Total.
Not inoculated:			
Total	829	4,477	5,306
Infected	16	15	31
Inoculated:			
Total	137	157	294
Infected	..	1	1

The one case which was infected after the inoculation was found to be a member of a family, one member of which had been suffering with pest pneumonia, and the patient had been infected previously to the inoculation, eruption being only delayed by the inoculation of the serum, and we are glad to add here that she is now on a way to recovery, though the case was one of the pest pneumonia.

In such instances the value of the serum inoculation as prophylaxis has apparently been proved.

For treatment of plague patients two methods may be recommended, the one requiring operation or extirpation of buboes, and the other the inoculation of the serum. Efficiency of the treatment depends on the stage of plague developed; when performed at an early stage a favorable turn may be expected, but in the later stage, especially when the patient develops septicæmia, the treatment becomes futile. Hence it is important for physicians to diagnosticate patients at the earliest stage possible. The good result to be obtained from the serum treatment admits of

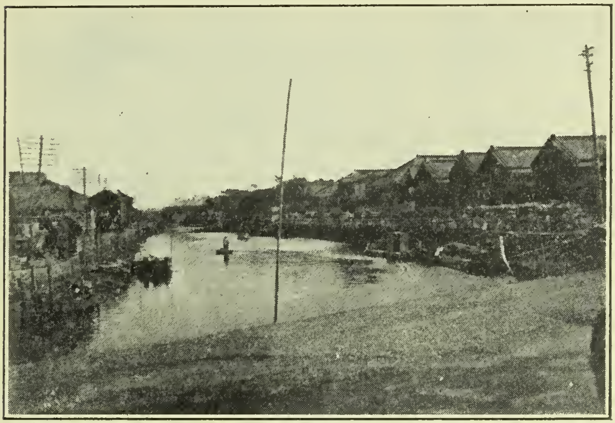

FIG. 7.—Warehouses inclosed by a zinc wall.

no dispute. During the first outbreak in Osaka Yersin's serum was used for inoculation. but owing to the scarcity of the supply results fell short of expectations. Since 1900 our institute commenced the preparation of the serum to meet the constant demand. For the patients actually suffering from the plague a comparatively large quantity (200 to 240 c.c.) of the serum ought to be used. Although we are not in a position to ascribe to the pest serum such absolute effectiveness as the diphtheria serum has, we have no doubts as to the value of the former remedy. The following fact illustrates most closely the value:

A series of experiments was conducted in an isolating hospital in Tainan, Formosa, with a view of comparing the results of serum inoculation with those of extirpation of buboes and systematic treatment. Of the fifty-six patients operated on, thirty-five (62.5 per cent.) died, while out of the same number of patients treated with the serum death rate was 34 per cent. From these experiments it is seen that the power of the serum reduced the death rate considerably.

That the most effective way to save the patients is to resort to both serum inoculation and extirpation of buboes at as early a stage as possible has been demonstrated by the experiences so far obtained during the epidemics in Japan.

Rats as Propagators of Plague.—The fact that the rat is closely connected with the plague outbreak at all times and places has been evidenced and admits of no dispute. The epidemics in Japan have been invariably traced to this animal. Obviously rats have a high susceptibility to plague; their habits, too, brings them constantly in contact with filth which conveys the plague germ; and they feed upon one another. These facts must favor to spread the plague. The discovery of human victims of pestilence is almost invariably preceded by the discovery of the plague infected rats. Hence, the killing of rats must be resorted to as the first and most important step in the prevention of the epidemic. In the first epidemic in Osaka and Kobé the ravage was gradually stopped by urgent efforts directed at the destruction of rats; and that in Tokyo and Yokohama was confined to a small area by the strict enforcement of rat killing measures. The number of rats killed in Tokyo since 1900 up to date amounts to the enormous figure of 4,820,000, that is to say, an average of 800,000 a year. In other words, if these dead rats were laid side by side they would fill the length of seventy-five, miles. The price paid by the local government for these rats, which are bought from the people, as aforesaid, amounts to 160,000 yen, that is, in Tokyo city alone.

The rat tribe, however, increases at an enormous rate. In a month after pregnancy more than five young ones are, as a rule, born from a single pair. Each young rat reaches puberty and pregnates at the age of three months. They thus multiply by geometrical progression; and if rats be destroyed by artificial means the destruction only lessens the struggle for existence, and the rate for multiplication redoubles. In Tokyo more than 4,800,000 rats have been killed, yet we can hardly notice any considerable decrease in the numbers of the animal.

For killing rats in Japan, such poison as arsenic and phosphorus, together with traps, are chiefly used. As the Daniz's bacillus, which may be effectively used for killing field mice, has been found futile for house rats, we do not use it now.

As to the disposal of rats for plague prevention some one has offered the following suggestions: The rats most prevalent in human habitations belong to the species of *Mus rattus*, which unfortunately is most liable to be attacked by plague. There are others, however, belonging to the species *Mus decumanus*, which has a comparatively great power of resistance against plague. The latter species is a great enemy of the former, hence by letting *Mus decumanus* increase its number the plague conveying rats could be greatly extinct. Such a suggestion appears to be impracticable, for from my actual observations it is evident that so far as the epidemic in Japan is concerned the kind of rats has had very little to do with propagating plague. The result of zoological researches, moreover, tends to confirm the fact that, although there are found these two species of rats distinctly marked, the rat most prevalent in Japan is a mixed race between the two, which is also susceptible to plague. Such facts rather contradict the assumption that the two species are natural

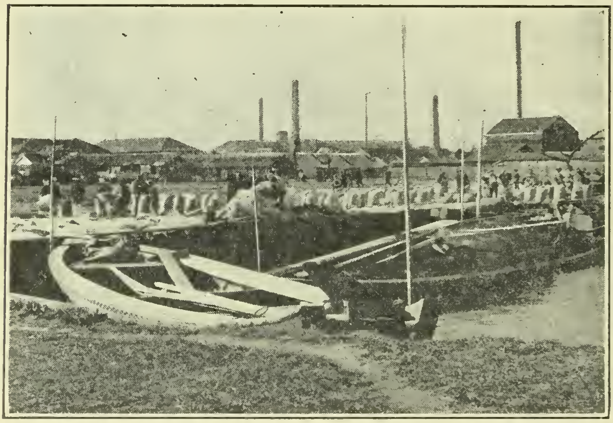

FIG. 8.—Disinfecting pouches of rice by exposure to sunlight.

enemies to each other. The suggestion, therefore, can hardly be made the basis of plague preventive measures.

The best way to treat rats in connection with plague preventives is not to permit them to remain or to expel them from human habitations. For this purpose I suggested that all buildings be rebuilt according to a proper plan. This particularly applies to the Japanese house, which is in most cases built of wood, as such buildings are liable to give quarter to rats. I understand that San Francisco is planning a reconstruction of its Chinese town. I most highly approve of such a step in view of the situation of that port, which is constantly threatened with an intrusion of plague. In several tropical countries, too, the cause of the recent fortunate decline of plague epidemic may, I believe, be attributed chiefly to the rebuilding of the cities since they came into possession of a civilized nation. In Japan such

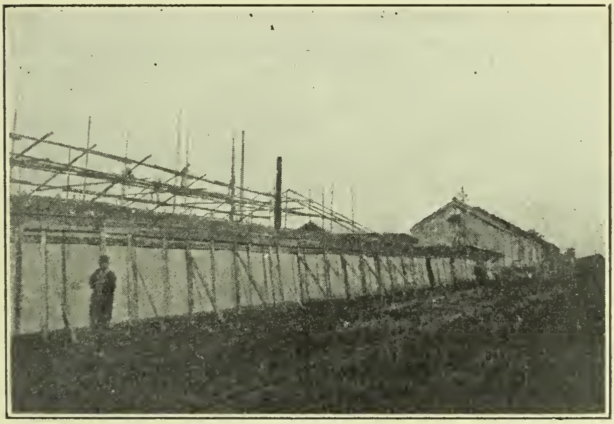

FIG. 9.—Zinc wall.

insular territory as Formosa, which has been invaded by the plague, is now being attended to by the sanitary officials, and the buildings in the central part of Taihoku city have been reconstructed so as to keep the rat tribe out. As a consequence the ravages of the pestilence are now practically confined to the villages or groups of unsanitary habitations belonging to the natives, who live with the rat tribe, and permit the animal to flourish.

The following table demonstrates the fact that during a plague epidemic the number of infected rats found runs parallel with that of the patients discovered:

	Osaka.		Kobé.	
	Patients.	Infected rats.	Patients.	Infected rats.
May	1	0	0	2
June	0	0	0	0
July	0	0	0	0
August	0	0	2	3
September	0	5	8	1
October	6	39	4	17
November	45	119	36	151
December	82	634	40	405

The number of rats examined last year in Osaka amounted to 1,195,116. Of these nineteen infected rats were found previous to May, making the total of 816 infected rats. In Kobé 553,616 rats were examined, of which the number of infected rats found were 579 as in the table. From these it may be inferred that the frequency of infection bears a direct proportion to the number of infected rats found, and that the extent of the epidemic may be approximately known by the extent of the localities where infected rats are found.

Our attention is particularly directed to the fact that the fiercest ravages in every epidemic are found in winter rather than in summer. This may be due to the resistance offered by the plague germ to cold and dryness—nevertheless it appears to be a point needing consideration.

A particularly interesting fact is that both in Osaka and Kobé the number of infected rats found during the last two months of 1905 was a considerable one as compared with the number of plague patients. Also the statistics up to the end of January, this year, have this remarkable feature: that there were 481 infected rats against six patients in Kobé, and 430 infected rats against sixteen patients in Osaka.

On the occasion of the present epidemic I had an opportunity to make close observations on the prevalent conditions, and discovered an interesting fact concerning the habit of the rodent. Rats generally live on the ceiling below the roof, but in winter they change their abode. Their winter abodes are in the ground just below the floor. The ground is dug one foot or two deep; and the openings on the surface give us a hint as to where the rat killing sanitary measures should be applied. When such openings are dug out and examined, rats in considerable numbers are invariably found. It appears that the rodent, like some lower animals, adopts a subterrestrial life in winter. And as their habit is gregarious and far away from human beings, if a number of dwellers in common are exposed to an infectious disease, a great number must fall victims of the contagion, while the occasions of infection for human beings are relatively much fewer. Again, as it is a habit of rodent that the weaker are constantly menaced and frightened by the stronger, those that have been weakened by the plague have to be constantly on the watch against pursuers, and as the weakened rats have no strength to climb fences or mount to any considerable height, they are obliged to wander about the surface of the ground. This gives the cause of the large number of infected rats as compared with human patients during a winter epidemic.

It is apparent that the rat killing measures must of necessity involve application of biological knowledge bearing on the rodent. Our knowledge in this respect is yet to be perfected. The rat killing methods of to-day consists of poison and traps. Such methods have only a temporary effect, and cannot be taken as a means of permanently rooting out the evil. As is well known, the destruction of rabbits in Australia had a permanent effect, and we have much to learn from the method involved. It was based on the fact that the rabbits are polygamous animals, and that if therefore as many females as possible be destroyed by artificial means, there will, therefore, be a struggle among males for the possession of females. The result of such a practice cannot of course be expected in a brief period, nevertheless it is of a permanent character. I suggest that something of this nature be planned for the destruction of the rat tribe.

Conclusion.—In conclusion I should like to suggest here what I consider as an ideal plan for fighting plague. I believe that the fatal pestilence, however obstinate in its ravages and terrible in its effects, can be fought and vanquished by the persistent efforts of man. I also believe that where human endeavors backed by money are determinedly directed against any object, nothing can remain unyielding. But the efforts, however laborious, and the money, however vast, can be of no value unless they be accomplished by wisdom—I mean the application of the scientific knowledge. The danger of intrusion of plague through open ports must increase in proportion as international commerce progresses and maritime enterprise advances. Again, where man fixes his abode the rat tribe accompanies him to share it; and the unwelcome creature becomes the cause of the dreadful evil. In ports where vessels from infected regions frequent, an epidemic of pestilence may not be difficult to fight out. But if it should be that ravage after ravage is going to be spread through fresh cause of importation, the task becomes rather cumbrous. involving the expenditure of vast amounts of money and tedious efforts. In regions like India and South China plague appears to be deeply rooted, prevailing almost incessantly for several years, and producing each year more than 200,000 patients. It is apparent that we cannot avoid the danger of intrusion of the pestilence at any moment so long as we do not cease intercourse with these regions. To be content with merely placing quarantine on the incoming vessels from these places, or enforcing rat killing sanitary measures in the open ports, seems to me a very poor means. Why not extend them to the source of the danger and destroy the cause of the evil permanently? Plague is not only objectionable to the people of one locality, but it is an enemy of mankind. All the civilized nations have to fight this common enemy. I believe that there ought to be an international conference to discuss a plan, collect money, and organize an international army to fight and vanquish this disease from the surface of the earth. The expedition should be sent to the regions of India and South China. The expense needed for such an enterprise would be only a small part of what the civilized nations are spending for their armies and navies; or the money spent in every country would suffice for the preventives of the pestilence.

MOSQUITO WORK IN RELATION TO YELLOW FEVER ON THE ISTHMUS OF PANAMA.*

COLONEL W. C. GORGAS, M.D.
Assistant Surgeon-General, of the United States Army,
and Chief Sanitary Officer, Canal Zone.
ANCON, CANAL ZONE.

I shall confine myself more particularly to the question of yellow fever and malarial fever. While we have to deal with all tropical diseases on the Isthmus and to establish a health department such as any community of the same size in temperate zones would be obliged to have, these two diseases, yellow fever and malaria, were the great ones that have caused the principal mortality in the two great works before undertaken down there, namely, the building of the railroad and the attempted construction of the canal by the French. The conditions were much the same as had confronted us in Havana, with the exception that in Cuba we had for two months in the year cool weather during which mosquitoes bred scarcely at all; in Panama there is no difference of season except that between the wet and dry season, and mosquitos breed as readily in January as in July. Another difference is that at Panama we have a country district of 50 miles in extent to guard against malaria troubles; in Havana we merely had the suburbs of the city to attend to in this respect.

During the French occupation the heavy mortality among their European employés had been a potent factor in the failure of the canal work. It is difficult for us to get statistics that represent exactly the losses under the French. Their work was done under the contract system, the canal line having been divided up into seventeen divisions and let to seventeen different contractors. These contractors were charged a dollar a day for every sick man to be taken care of in the hospitals of the French company. The tendency would be, therefore, when a man became sick for his employer to discharge him so that he would not have to bear the expense of his care. The French company were building a canal through the Columbian territory, just as the Pennsylvania Railroad built its track through Pennsylvania; they had no police control whatever of the territory along the canal. They had no means of telling how many of these employés of the contractors died along the line. All that they could know was that so many reported for work each day; what became of the others they had no means of telling. At their large hospital, Ancon, they kept very accurate statistics, and the number of deaths that occurred there can be safely quoted as entirely correct, but it leaves a very great limit of uncertainty as to what portion were treated in hospital and what proportion died along the line. The English consul, who was down there during the period of construction, is inclined to think that more deaths of employés occurred out of the hospital than in it, and he had very good opportunities for judging. Nine-tenths of the laborers were Jamaica negroes, English subjects, and looked to the English consul for care and protection. The consul tells me that he personally knows of a great many being found dead along the roadside while endeavoring to find their way to him in the City of Panama, and some even dying in his office. On the other hand, the old French superintendent of hospital, Dr. La Croisade, who is still with us, thinks that the hospital statistics represent most of the deaths.

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* Address delivered before the American Society of Tropical Medicine, Dec. 8, 1905.

It seems to me, both from what I can find out as common opinion on the Isthmus, and what would seem to me to be human nature under the circumstances, that it is a fair conclusion that the French statistics represent not more than half the mortality that actually occurred. And in quoting these statistics I will ask that this be borne in mind.

The United States Government took over the canal property in May, 1904, but for various reasons there was considerable delay in getting sanitary work fully started, and the authority for doing sanitary work in the towns of Colon and Panama was not granted till toward the latter part of February, 1905. We then built up much the same organization here that we had developed in Havana. All cases of yellow fever were required to be reported to the American health authorities, and, in addition to this, all cases of fever of any kind occurring in an American were also required to be reported. It was a considerable advantage to us in Panama that the equipment of our hospital allowed us to give very much better nursing, care and medical attention to all patients than could be obtained elsewhere on the Isthmus. For this reason, Americans generally reported to the hospital when they had fever of any kind, and we usually got cases of yellow fever within the first day or two of the disease. This resulted favorably to the patient as well as to the sanitary authorities; while the general mortality was about 25 per cent. of all cases, the mortality of the Americans treated in our hospitals was not more than 10 per cent.

As soon as we took possession of the hospital, we had two wards thoroughly screened and equipped for keeping out mosquitoes, just as had been in our wards in Havana. The suspected patient, when brought up, was placed in one of these wards. It is interesting to see what entire confidence all of our people soon acquired in the mosquito theory of the transmission of this disease. Ancon Hospital is beautifully situated on the side of the Ancon Mountain overlooking the City of Panama and the Pacific Ocean. It is pleasantly laid out in graded roads and paths beautified with tropical shrubbery of all kinds, and embowered in a grove of rubber trees and royal palms. Twenty years ago, under the French, it soon became infested with yellow fever, and every poor Frenchman who came in from whatever cause contracted yellow fever, and more than half of those who contracted the disease died. I was informed through the old superintendent who was in charge at the time that in one day they lost from yellow fever three of their medical staff and in the same month nine of the same body. Of the 36 sisters whom they brought over as female nurses, 24 died of yellow fever. One of the chiefs of our supply department who came over in the early French days told me that he was one of 18 young French engineers who came over in one vessel; that in a month after their arrival all had died but himself. I am merely mentioning these details to show how different the circumstances are at present.

For nearly two years now we have constantly had yellow fever in these wards; the nurses and physicians are all non-immunes, yet not a single case of yellow fever has been contracted in this way. The nurses never seemed to consider that they were running any risk in being with yellow fever cases night and day in these screened wards, and the wives and families of the officers connected with the hospital lived about the grounds in all directions with the knowledge that yellow fever is constantly being brought into the grounds and treated in the buildings contiguous to them. I do not say this at all in criticism of the French. Under the same circumstances twenty-four years ago I doubt if we could have done any better, but the knowledge acquired by Reed's board and Finley's persistent propaganda have enabled us absolutely to exclude all probability of any contraction of the disease in our hospital. An American sick from any cause at Panama has no fear whatever of being treated in the bed next to that in which his companion is being treated for yellow fever. Dr. Carter and I live in the old ward used by the French for their officers. In this building, I suppose it is safe to say, more men have died from yellow fever than in any other building of the same bed capacity at present standing. We have our wives and children with us. Ten years ago I would have thought this the height of recklessness, but to-day, by taking precautions which are now recognized in yellow-fever work, we all look on ourselves almost as safe as we would be here in Philadelphia. In the yellow-fever wards the additional precaution is taken of putting each new patient in a wire cage just large enough to cover his bed. Here he is kept until the infectious period of the disease has been passed. Of course, in so important a matter as treating yellow fever in a general hospital, no possible chance of the spread of infection can be taken, so that in addition to every possible measure for keeping mosquitoes out of the ward and away from the yellow-fever patients, we also fumigate these wards every two weeks, so that if a mosquito should get in and bite a patient she would not have time to become herself infected. You will recollect that a period of time of from twelve to fifteen days has to elapse from the time that the female stegomyia bites the yellow-fever patient till she herself becomes infected and is able to convey the disease; therefore, if we fumigate every two weeks we could catch all mosquitoes before they had time to do harm.

The case having been reported in the city and the patient having been removed in a screened ambulance to the hospital, orders would be given from the central health officer to the proper fumigating brigade to fumigate this house and all the contiguous houses, with the intention of killing the mosquitoes who gave the disease and also those that had bitten the yellow-fever patient, and if left alone would become dangerous in a couple of weeks. The stegomyia is a very domestic mosquito and generally does not leave the house where she is born and bred and does not stir much from the room where she has lived; probably the fumigation of the house itself would catch all infected mosquitoes, but as an additional precaution the contagious houses were taken, so that if by accident an infected mosquito had drifted from her original locality she would be caught. The fumigating squads were composed of an experienced foreman and twenty men. They carefully pasted the house just as one would if one were going to disinfect with formalin. The fumigating material generally used was sulphur, sulphur being decidedly the best mosquitocide we have, but in many buildings, such as stores and the better class of residences, there are many articles that are seriously injured by sulphur. In such cases we use Persian insect powder, pyrethrum; but in the use of pyrethrum care has to be taken that the mosquitoes are swept up and destroyed immediately after the fumigation. If this precaution is not taken a few may revive and again become dangerous. The patient is not forced to go to the hospital if he does not so desire. If he elects to be treated at home, the central office is so informed and the carpenter squad, who have screens on hand prepared for this purpose, are ordered down and screen the patient in so that he is protected from mosquitoes and those that are in the room can not get out. Only one exit is left the room, a guard is placed who keeps the key of the door and only allows those in and out who are authorized by the physician. The fumigation in the rest of the house is then finished and the screened room is fumigated when the case has terminated.

As I have just stated, the stegomyia is a very domestic mosquito. She is very cleanly in her habits and breeds principally in clean rain water. In Panama the population have depended principally on rain water for domestic purposes, so that every house had cisterns, water barrels and such receptacles for catching and storing rain water. These we had to cover so that mosquitoes could not have access to them; for this purpose the city was divided up into small districts with an inspector in charge of each district. This inspector is required to get around his district at least twice a week and make a report on each building with regard to its condition as to mosquito breeding. All the cisterns and water containers in Panama have now been covered and in the water barrels spigots so placed that the covers do not have to be taken off when water is drawn. About the first of March, when the first inspections were made, in the neighborhood of 4,000 breeding places were reported. On the last of October, when the last inspection was reported just before I left Panama, less than 400 receptacles containing larvæ were recorded. This, I think, will give you a fair idea of the decrease in mosquitoes through the City of Panama.

In the City of Panama we found by count that 90 per cent. of the mosquitoes were stegomyia. This is another point in which we greatly differed from Havana. In Havana we found by count that only about 5 per cent. of the mosquitoes were stegomyia.

This about covers the ground of the methods adopted for controlling yellow fever. Of course, you can see how very important it is for us to get hold of every case of yellow fever as it occurs; particularly is this the case at present, when it has about disappeared. The governor has offered a reward of $100 for any case of yellow fever reported to the authorities. Between Panama and Colon there are some twenty villages running from 500 inhabitants up to 3,000; yellow fever in the last year has occurred at several of these villages. A queer thing about yellow fever is the fact that the natives in a locality where it frequently occurs are entirely immune, so that in these small towns it is only the American employé who can have yellow fever. They usually live in frame buildings, well separated from the surrounding buildings, and it is a very simple thing to fumigate such buildings at once when a case occurs, and to get rid of the disease. We have not had a single instance of failure in disinfection in any of these small towns.

The results of this work have been the apparent elimination of yellow fever. In June, on the zone, we had 67 cases, in July 40 odd cases, in August about 27 cases, in September about 7 cases, in October 3 cases, and none in November and none so far in December. In the town of Colon our last case occurred July 23. Of course, it would be too early to say that yellow fever had been entirely eradicated from the Isthmus. This can not be affirmed with any certainty until the full life of a female stegomyia mosquito has been passed since the last case. In Havana, at Las Animas, we had a female stegomyia mosquito live in captivity for 150 days. So I think we ought to let at least two months pass without a case before we can say with any certainty that yellow fever has been eliminated. The same measures for the control of yellow fever and the extermination of the stegomyia mosquito were taken at Colon and at the various places along the line of the canal. While yellow fever has a great moral effect on the force, and was more important from this point of view to us than any other disease, malaria was the disease that had always caused the greatest loss from disability, that is, in a large force of men more days were lost from work on account of malaria than probably from all other disease put together.

My paper has already extended to such lengths that I can not go into a detailed description of the measures taken against malaria. They were the same as those outlined at Havana, and that are now so generally in use in the United States, principally superficial ditching. The results have been as satisfactory as they were in Cuba. In October we had a force of 22,000 men on our pay roll; of this number 21 per thousand were sick daily. This is an exceptionally small sick rate, very much less than is the average for our army in the Philippines. I think it safe to say that we are now digging the canal with as little trouble from sickness as would be the case if a similar number of men were engaged in a similar project between Philadelphia and Baltimore, and I see no reason why this rate should not be continued or even improved on. Water supplies are being put in, sewage systems constructed, houses repaired and built, food supplies and cooking arrangements constantly improved.

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ON ORNITHODOROS MOUBATA, MURRAY: A DISEASE-BEARING AFRICAN TICK.

BY F. C. WELLMAN, M.D.

[Published under the imprimatur of the American Society of Tropical Medicine.]

INTRODUCTION.

It was on the occasion of my first visit to Angola several years ago that I made the acquaintance of the tick mentioned in the title to this paper, but I only began to study it specially during the course of some researches concerning human spirillosis undertaken in 1904. While investigating this disease I naturally sought information regarding the tick which undoubtedly transmits it in this region, and stray notes on the history, metamorphosis, habits, and morphology of the animal (part of which has appeared from time to time in different journals) have collected until it has seemed that they may be of sufficient interest to publish as a whole.

NAME.

The native name for the tick in Angola is "Ochihopio," and probably has reference to the burning sensation following on its bite, or possibly to the fever which is caused by it. The scientific name, which, for reasons given later (*vide infra* "Historical Note"), should be adopted, is *Ornithodoros moubata* Murray (1877).

SYNONYMS.

Argas moubata Murr., 1877 (Journal of Travel);

Ornithodoros savignyi var. *Cæcus* Neum., 1901 (Mém. Soc. Zoöl. France, xiv, 1901); *Acarus moubata*, Kufu, Mbu (Tete); Tampao, Garrapato (Portuguese); Karapatti; Lirvuns (Bantu).

HISTORICAL NOTE.

The first mention of *O. moubata* in scientific literature was the description of some specimens collected in the colony where this is written (Angola) by Dr. Friedrich Welwitsch, whose admirable collections of the plants of Lower Guinea have made his name well known to all botanists. Neumann described in 1901 a tick which he admits to be synonymous with this species under the name *O. savignyi* var. *Cæcus*, but I prefer to retain the name *O. moubata* Murr., as the tick under discussion seems to be clearly different from the original *O. savignyi* Aud., of Egypt, Somaliland, and British East Africa, first described from Egypt in 1826 (although sometimes known as *O. morbillosis* Gerst., 1873), and was, as has been shown, discovered by Dr. Wilwitsch and described by Andrew Murray in his Journal of Travel nearly a quarter of a century before Neumann's description was published. Dr. Livingstone was the first to describe the disease to which the tick gives rise. He met the condition in Portuguese Southeast Africa. Later Sir John Kirk and Drs. Dowson, Daniels, etc., verified Livingstone's observation. The writer has recently described the disease from Angola, where the tick was first found. Ross and Milne in Uganda were the first to definitely establish the connection between tick fever and spirillosis, and their announcement has been confirmed by Dutton and Todd on the Congo.

BIONOMICS.

Habits. The Ochihopio tick is a veritable pest throughout the whole of Angola. They infest the huts and camps of the natives in great numbers. I have found as many as a hundred in an hour in an old native hut. In some places they become an intolerable plague, and the blacks are not seldom compelled to burn their old kraals and build new ones in order to escape them. They hide (like the bedbug, *Acanthia lectularia* L.) in the thatch and cracks of shelters and houses and come out at night to bite. They bite both man and all domestic animals. I have found as many in pigsties as in any other one situation. When ready to bite, the animal fastens itself to the skin of its host by means of the double hooks on its legs and inserts first its mandibles, followed by the hypostoma, until the rostrum rests against the surface of the victim's skin. When satisfied, by which time it has increased to ten times its original weight, the tick drops off, and, if a female, seeks a place to lay her eggs. The feces voided after feeding are white. Unlike some ticks, *O. moubata* lives for years and preys on an indefinite number of hosts. It is tough and somewhat difficult to kill. When placed on its back on a smooth surface which affords no hold for its legs, such as a piece of glass, it has a curious fashion of contorting its body to enable it to roll over. When touched or otherwise disturbed while moving about it folds up its legs and remains motionless for a short time. Compared with other acari the Ochihopio is fairly active in its movements. If placed, however, in a covered dish the ticks will, after an initial attempt to get free, remain quiet for days at a time, only moving if the dish, or table on which it rests, is struck.

Life history. The following is a sketch of the life history of *O. moubata* as observed by the writer in Angola: The ticks were fed on the blood of a young pig. Copulation was seen in two instances, the ticks grasping each other with their legs and approximating the dorsal surfaces of their bodies. Two large impregnated females were placed in a covered glass dish in which was a handful of dust from the floor,[1] into which the ticks immediately burrowed. They were given no food and examined frequently. It was nearly two months (57 days) before any eggs were laid. The first batch of eggs laid by tick No. 1 numbered 49, the parent "setting" on them for two days (until I turned her over to examine the eggs) as if to incubate or protect them. The second batch, laid by the same tick the day after I removed her from the lot of 49 eggs just mentioned, numbered 29. She also "set" on these for four days. Although unmolested she had abandoned them on the morning of the fifth day. Tick No. 2 behaved similarly, except that she did not begin to lay for a week after her companion had finished, and that she laid three batches of eggs, which numbered 28, 41, and 19 respectively, or in all 88. The eggs are black, round, measure 800 to 900 microns in diameter, and adhere together, looking not unlike a tiny bunch of grapes. The history of the eggs was as follows: At the end of one week differentiation of the egg contents could be made out, and the larvæ could be definitely seen a few days later. No movement was observed. On the fifteenth day there emerged from the shell, not larvæ but octopod nymphs. The exuviæ of the larvæ are probably left by the nymphs in the shell of the egg. As the nymph grows it gradually becomes of a yellower tinge, until the time of its next moulting, but when it exuviates the new shell appears to be more of a greenish hue. In moulting the skin first splits around the edge of the body and the tick crawls out. After this ecdysis is complete the exuviæ may be seen lying about. They are of a pale-yellow color and perfect casts of the acarus. The adults vary greatly in size. They seem to attain greater dimensions in some localities than in others. The largest individual I have measured was about 11 millimeters in length after having gorged itself with blood. It has been stated that the female lays her eggs shortly after feeding and then dies. As I have mentioned above, nearly two months elapsed between the feeding of the ticks used in my observations and their ovipositing, and both females have been kept to date without food (eleven weeks since laying their eggs) and are still alive and active.

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[1] Dust or sand used for such experiments should be first sterilized by heat. In the observation I am detailing eggs of another species of tick (which has been forwarded to the British Museum for determination) were overlooked, and its free hexapod larvæ were at first taken for those of *O. moubata*, and caused great confusion and fallacy until I finally separated the nymphs.

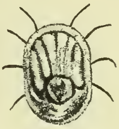

Fig. 1.—*Ornithodoros moubata* Murray. Female, dorsal surface. Large adult. Natural size.

Enemies. An interesting question is that of the parasites and other enemies of the tick I have studied. In one locality in Bihé district I observed a fungus which sometimes attacks and destroys them. The disease generally begins at one edge of the tick and appears in the form of a light, almost white spot which spreads. The infected ticks are more sluggish than healthy ones. Later, bearing in mind that *Acanthia lectularia* is sometimes mulcted of its ingested blood by another animal, I continued my researches on the enemies of *O. moubata*, and discovered an insect which preys on them, catching them and sucking by means of its powerful piercing proboscis the blood with which they have filled themselves. This insect (called by the natives Ochindundu—"the striker") is entirely black except the first two pairs of legs, which are bright-red and provided with curious paddle-like structures, evidently designed for holding securely the tick upon which it feeds. I shall not attempt a detailed description of the "Ochindundu" here, as a specimen has been sent to the British Museum for determination, and it is hoped a report on it will soon be received. I have watched the "Ox Bird" (*Buphaga africana*)

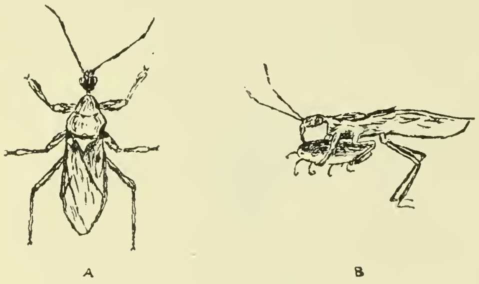

Fig. 2.—The Ochindundu. A, dorsal surface; B, side view, showing the position it assumes in the act of sucking blood from an Ochihopio (*O. moubata* Murray). Natural size.

and also a white egret picking ticks off of game and cattle. Whether *O. moubata* has a special vertebrate enemy or not I have not learned.

SYSTEMATIC POSITION.

Ticks belong to the class *Arachnoidæ*, order *Acarina.* In this order the *Ixodinæ* are divided into two sub-families, the *Ixoda* and the *Rhipicephala*, each of which contains several genera. The *Argasinæ*, however, to which belongs the tick under discussion, consist of but two genera, *Argas* and *Ornithodoros.* The Argasina are known by having the rostrum inferior, and both dorsal shield (scutum) and pulvilli of tarsi wanting. A synopsis of the family is as follows:

Argasinæ—
(1) Body usually flat; thin at edges; without deep ventral grooves; eyes absent..*Argas.*
(2) Body thick at edges; ventral grooves anal, preanal, and postanal; eyes sometimes present......................*Ornithodoros.*

DESCRIPTION.

Fam. *Argasinæ.*

Ornithodoros moubata Murray (1877).

Body thick and rounded at the edges. Tips of palpi not visible from above. Preanal grooves we marked. ♀ larger than ♂, but sexual dimorphism not striking. Color brown. Eyes wanting.

♀. The body is deeply furrowed both on the dorsal and ventral surface. In younger specimens the furrows are much less marked, especially on the ventral aspect. The shape of the body, which is thick and rounded at the edges, is roughly oval, flattened, and with the dorsal surface more rounded than the ventral. The tegument is finely mammillated, giving it a leathery appearance, the shagreening extending over the entire surface of the tick. Scutum absent. Rostrum inferior, close to anterior margin of body, and hidden from above by a projecting fold of the tegument. Palpi free, short (tips not visible from above), filiform, four-jointed, and placed on either side of the haustellum. Close scrutiny of the supracoxal fold of the first pair of legs fails to reveal any trace of eyes. Anus half-way between middle and posterior margin of ventral surface. Preanal grooves deep. Sexual opening nearer anterior margin than middle of ventral surface,[1] lying behind the haustellum. Tarsi without pulvilli, legs ending in two simple hooks. A few minute bristles are scattered over the surface of the tick, varying greatly in number and position in different specimens. Color ranges from yellowish-brown to dark, greenish-brown.

Var. *a.*—Dark yellow.

Var. *b.*—Dull gray.

Lat. 6–7 mm.

Long. 8–9 mm.

Habitat. Bihé, Angola, W. Africa (5200 feet). Neumann records it from Angola and many other African localities, ranging from Egypt to the Transvaal. He remarks concerning it "*paraît bien plus commune que le type*[2] *pourvu d'yeux.*"

Observations. The above description, which is doubtless very imperfect, was drawn up (the writer not having access to the published descriptions) from several adult female ticks collected at Bihé, February, 1905. One of these was sent to the

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[1] Not including the projecting hood of tegument which conceals the capitulum when the tick is viewed from above.

[2] *O. savignyi* Aud.

British Museum and pronounced to be " identical with specimens in the Museum labeled *O. moubata* Murray."

ANATOMY AND PHYSIOLOGY.

Only a preliminary dissection of several ticks has been made as yet. The common ganglionic mass (brain), alimentary canal with its diverticula, etc., are well seen. The mouth parts too are of great interest, but a description of these with the internal anatomy would make this paper too lengthy, and must wait till a future occasion for consideration. Several physiological questions connected with their tenacity of life, longevity, power of existing without food for almost incredible periods of time, etc., are of the greatest interest. The mechanism of digestion is another question of importance. While feeding, and for some time afterward, a whitish secretion which when dry resembles whitewash escapes as feces from the anus. The elaboration of this, whether within the cells of the ventriculus or in the Malpighian tubes, is a point for study. It has been stated that the cells named when the tick is filled with blood change their shape, allowing the passage of the digested food into the body cavity and finally into the lumen of the ventriculus, but that the cells still retain a certain residue of crystals or concretions from the excreta. It is hoped that full investigations on these questions and the exact method of transmission of tick fever, whether mechanically or by a metamorphosis of the parasite in the tick's body, will be made by those in a position to solve such problems.

PATHOLOGICAL IMPORTANCE.

Ixodiasis (even that due to one acarus) is a subject too extensive to be more than touched upon in such a paper as this. I have on several previous occasions discussed at some length the rôle of *O. moubata* in the dissemination of spirillosis, and a few brief notes on tick-transmitted diseases must suffice here.

The bite. The bite of the tick is very painful, as I can personally testify, the swelling and irritation (in the case of Europeans especially) not subsiding for days. The wheals are hard, raised, and itch and swell most disagreeably if scratched, and this even a week after being bitten. The bite of young ticks (nymphæ) is said by the natives to be more severe than that of the adults. I have experi-

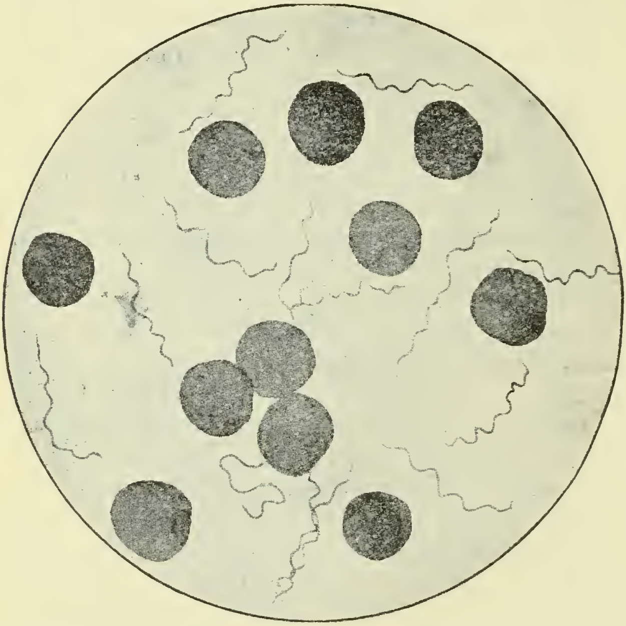

FIG. 3.—*Spirochœte obermeieri.* The parasite of relapsing fever, carried by *O. moubata.* Blood film from the author's case.

mented on my own person with the ticks, and am convinced that this is generally the case.

Tick spirillosis. In another paper I have shown that microscopically verified spirillary fever has been reported from such widely separated regions as South China, Sumatra, India, Europe, America, and various quarters of Africa (Angola, Uganda, etc.). Ross and Milne in Uganda demonstrated in November, 1904, the characteristic spirillum in several undoubted cases of tick fever; the writer showed by charts, etc., published in April, 1905, that the disease is clinically identical with relapsing fever, both in respect to the temperature curve and the incidence of the parasites in the blood; and at the last meeting of the British Medical Association Dutton and Todd confirmed all these observations, and in addition showed that the parasite may be transmitted by the bites of young ticks hatched from eggs laid by infected parents (which has its analogue in the transmission of Texas fever of cattle), and that it is only uniformly pathogenic to man and monkeys. This parasite, which is a spirochæta rather than a spirillum, is morphologically identical with the parasite of the relapsing fever of temperate climates (*S. obermeieri*), but arguing from biological analogy one expects that it will prove to be different from those carried by other hosts. In view of the work of Schaudinn and others the probability of its being related to the *Flagellata* occurs to one. In my first case the parasites were very plentiful during the attacks of fever, but in a subsequent case they were much fewer in number. They measured on an average about 30 by 0.1 microns. I failed to observe multiplication in the condensation water of hemoglobin agar, and the cultures died out in a few days. The incubation period from the time of being bitten by an infected tick to the onset of the disease is said to be about a week. The symptoms vary. In my case above referred to I noted no rigor or vomiting, but there were pains in the back and limbs, malaise, and the temperature and sudden recovery were entirely characteristic of relapsing fever. That immunity may be acquired is proven by the fact that my second case of infection with the parasite showed no symptoms whatever.

Other Possible Rôles of O. Moubata.—The suggestions of Christy and the statements of Feldman as to this tick being an intermediate host of *Filaria perstans* have yet to be critically examined. The inference that blackwater fever may be due to a human piroplasm carried by ticks also deserves consideration.

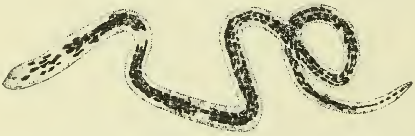

FIG. 4.—*Filaria perstans* Mans. Possibly transmitted by *O. moubata.* Blood of West African negro. Author's case.

OTHER NOXIOUS ACARINES.

Ticks with severe bites producing painful symptoms have been reported from different countries. *Leptus autumnalis* is too familiar to need mention. *Trombidium thalsahuate* from Mexico also causes trouble, especially infecting the eyelids, axilla, navel, etc., and the fatal flood fever of Japan (Akamushi or Kedani) is said to be caused by a mite similar to the above. Again, the so-called "Atriplicism" of China is said by some to be due to a mite which lives on *Atriplex littoralis* and not to the poisonous effects of the plant itself. *Tetranychus molestissimus* of Argentine and Uruguay is credited with causing a skin disease accompanied by fever, while *T. telarius* causes pustules and swellings, and *Pediculoides ventricosis* is known to set up erythema, itching, swelling, and fever. While the claim for *Dermacentor reticulatus* as the carrier of the parasite of spotted fever has not been substantiated, yet the suggestion is one of interest. *Argas persicus* is, of course, the classical instance of a fever-producing tick. *Argas reflexus*, although generally found on pigeons, may infect man and cause angry erythema and edema. The bite of *Ornithodoros turicata* in Central America is very severe and not seldom followed by grave symptoms. *O. talaje*, also of Central America, *O. tholozani* of Persia, and *O. megnini* of Mexico are all pathogenic to man. Other acarines have been known to invade the cavities and tissues of the body. *Tyroglyphus siro* and *T. longior* have been found in the urine and pus of man. *Glyciphagus prunorum* is not seldom found in the stools. The eruption occurring on the feet of coolies in Indian tea plantations, while generally attributed to rhabdite larvæ of *A. duodenale*, is thought by some to be caused by the presence of *Rhizoglyphus parasiticus*. Finally, *Nephrophagus sanguinarius* has been found in the urine of several fatal cases of hematuria in Japan and probably lives in the kidneys. Turning now to similar parasites infesting animals we find the list too long to even enumerate. Animal piroplasmosis, which is of the greatest economic importance, has been shown to be carried by ticks. One need only advert to *Piroplasma bovis* carried by *Rhipicephalus annulatus*, *R. evertsi*, and *R. auctralis*, and to *P. canis* by *Dermacentor reticulatus* and *Hæmophysalis leachi* in order to bring to mind the researches of Smith and Kilborne, Koch, Nuttall, Laveran, etc., on these subjects.

In conclusion it would seem that acarines as transmitters of spirilloses, piroplasmoses, and possibly filariasis and other diseases threaten to rival the *Culicidæ* in their importance to tropical pathologists. And while the study of tick-transmitted diseases has of late attracted a great deal of attention, still the subject is as yet in considerable confusion and further work is urgently required. It is to be hoped that medical men in the tropics will respond to the request of the directors of the British Museum and make and forward careful collections of the ticks infesting their districts, at the same time recording accurate observations regarding the transmission, symptoms, distribution, and parasitology of the tick fevers of men and animals which they may meet.

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* * *

NOTE ON AN INSECT FOUND BY DR. F. CREIGHTON WELLMAN PREYING UPON A TICK (ORNITHODOROS MOUBATA, MURRAY) AT BENGUELLA, ANGOLA, W. AFRICA.

The above insect is a specimen of *Phonergates bicoloripes* Stal, a species of bug (order Hemiptera-Heteroptera) belonging to the family Reduviidæ, the members of which are predaceous and as a rule prey upon other insects. The following is a brief description of Dr. Wellman's specimen:

Dimensions: Length 18½ millimeters; width of thorax at base of wings 5⅓ millimeters; width of abdomen (on which the wings when not in use lie closed one over the other like the blades of a pair of scissors) 5 millimeters.

Color, etc.: Thorax metallic purple; wings (which when closed conceal abdomen when insect is viewed from above) deep velvet black; hind legs bluish-black; front and middle femora and front tibiæ coral red, with tips of femora and base and tips of front tibiæ black; middle tibiæ brownish. The front and, to a lesser extent, the middle femora are swollen. The tips of the front and middle tibiæ are provided on the under side with large spongy pads, which enable the insect to obtain a firm grip of its prey.

E. E. AUSTEN.

British Museum (Natural History), London, S. W.
March 26, 1905.

Reprinted from the New York Medical Journal for August 4, 1906.

SOME CLINICAL NOTES UPON A RECENT EPIDEMIC OF DENGUE FEVER.*

By Aristides Agramonte, M. D.,
Havana, Cuba,
Secretary of the Board of Infectious Diseases, Havana, Cuba.

(Published under the imprimatur of the American Society of Tropical Medicine.)

The city of Havana and neighboring towns suffered a well marked epidemic of dengue fever during the second half of the past year. From the middle of September to the first of December, I attended one hundred and fifty-four cases and saw many others in consultation; more than three fourths of this number occurred in one of the suburbs (Vedado), where I reside, and which is thickly populated by the foreign element, chiefly American and Spanish.

It is impossible to determine with any degree of accuracy, what was really the extent of this epidemic; it was not until later that the sanitary department declared the reporting of cases as obligatory, and the epidemic was then on the wane. From information obtained, I am convinced that the disease existed in a latent form ever since the earlier part of the year, and even at this date, (March, 1906), and as a result of the recent yellow fever scare, we occasionally meet cases of dengue which are reported as suspicious of yellow fever. The question in my mind to-day is, whether the disease may not be endemic here, assuming epidemic form at long intervals.

As it has been observed in other epidemics else-

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* Read by proxy at the annual meeting of the American Society of Tropical Medicine, held at Philadelphia, March 24. 1906

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where, the one under consideration has practically exhausted itself without exhausting the material subject to infection; for, apart from the fact that it cannot be claimed that an attack of dengue confers positive immunity against subsequent infection, a large proportion of the population has not been affected by the epidemic.

During the period to which I refer, I have seen but few children attacked and no infants; or at least, the disease has not been recognized as such in the case of children less than five years of age. On two occasions, nursing mothers continued to suckle their infants throughout their attack of dengue, without causing any deleterious effect upon the little ones. One of these cases, a young American woman, kept up a fairly constant temperature of 40° C. (104° F.) during two days; nevertheless, the child, then three weeks old, was regularly put to the breast.

The degree of immunity conferred by an attack of dengue must be very slight or transitory. During this epidemic I saw four instances in which the disease reappeared upon the same individual, after an interval which excluded the possibility of their being relapses of the same infection; the periods between the two attacks varied from twenty to thirty-six days, and the second attacks were no less severe than the first; indeed, one of the cases to which I refer, after an interval of thirty days, presented most alarming symptoms the second time.

The mode of transmission is still a fruitful subject for speculation. Attempts have been made, by others, as well as myself, to infect individuals by the bites of mosquitoes, which had been previously applied to cases of dengue fever, at various intervals after sucking the presumably infected blood and employing several varieties of mosquitoes; according to reports, all efforts have been as unsuccessful as my own. This, notwithstanding the circumstantial evidence, is directly in favor of insect transmission, and I cannot but feel that mosquitoes are responsible for the extensive and rapid propagation of the disease, and further, that the inability thus far to demonstrate this theory must be due to some fault in the technics, which we are unable as yet to recognize and rectify. Finlay for twenty years defended the same theory regarding yellow fever, before we were enabled to demonstrate it. This epidemic coincided with the presence of a veritable plague of *Culex fatigans,* which particularly invaded the part of the city (Vedado) to which I have referred.

Dengue fever spreads very much like yellow fever; from house to house; along the same side of a street; attacking more the members of a family than the transient visitors, who do not sleep under the same roof, etc. Unfortunately, this is not the only point of similarity between the two diseases.

The next feature of interest which I wish to note, before discussing some strictly clinical characters, as I have observed them, is the period of incubation. In the midst of the epidemic, after the infected foci have been multiplied to a considerable number, it becomes actually impossible to trace the source of infection in any given case, particularly if the individual has resided within the epidemic zone for a period of weeks, or been travelling from one place to another. Some of the cases observed have led me to believe that from three to seven days elapsed from the time of exposure to the earliest manifestation of the disease, but the following cases indicate a much shorter period of incubation.

Mr. and Mrs. S. and two boys, twelve and fourteen years of age, respectively, arrived from New York on October 11, 1905, landing at 9 a. m., and reaching the home of Mrs. M., where they were to stop, at about 10 a. m. Mrs. M. and her daughter had recovered from a fairly severe attack of dengue from which they had suffered two weeks before. No fumigation or other disinfection of the premises had been carried out. On the 13th of October I was called to see one of the S. boys, who had been ill since the night before (thirty-six hours after reaching the house). The following day, in the evening (fifty-six hours after arrival), the second boy became sick and both went through their attack with well marked symptoms of dengue. One week afterwards Mr. S. developed a mild case of dengue. Previous to the boys' invasion, they had not been out of the house for any purpose.

We have here evidence of an exceedingly short period of incubation, (thirty-six and fifty-six hours). In other cases I thought to have seen equally short duration, but none of so striking and evident a character as the two above cited.

Cephalalgia, rachialgia, and fever, constitute a symptomatic trio, which may be said to usher in the attack in every case; their respective intensity varies, the back and bone aches being the most trying and unbearable. Some hours after the above symptoms develop, with intense suffusion of the skin, thirst, etc., the eruption may be observed in eight cases out of ten.

It is not my purpose in this paper to review the complete symptomatolgy of dengue as it has been constantly met with in all the epidemics heretofore described, but to remark upon a few clinical features which, in my opinion, have been treated with undeserved disdain or entirely overlooked.

The first of these, is the eruption previously mentioned. At the second to fourth day, the erythematous flush which may have been observed from the inception of the attack becomes changed into distinct eruption of a milliary maculopapular character, surrounding small irregular shaped areas of healthy skin, from one to three fourths of an inch in diameter, and which appear from a distance as pale blotches upon a reddish background. The eruption extends principally over the arms, breast, back and abdomen. It is not very apparent on the face, except sometimes about the forehead. In two cases the eruption was petechial in character, restricted to the wrists and hands, ankle and feet, extending to the palms and soles, respectively. In some cases the eruption lasts two or three days, perhaps four, but generally it remains plainly visible not more than forty-eight hours; in a great many instances it appears only for a few hours, making it possible to be overlooked by the physician or nurse. In the earliest stage the rash is seen only at the bends of the elbows and knees, or about the wrists or neck.

I have tried to describe the eruption as it has been most frequently met with; it cannot be said that it presents exactly the same characters in every case; the patients' complexion and surface conditions, I believe, have direct influence in modifying them. In the case of a plethoric blonde German woman, the eruption was like that of scarlatina; face and body intensely red, and the skin œdematous, raised in patches and hot to the touch. In the African and his descendants, the eruption is most puzzling; fortunately the colored races seem to enjoy a marked degree of resistance against dengue infection. Desquamation often takes place during convalescence; usually furfuraceous; more rarely in strips.

Albuminuria in a slight degree has been found in almost every case, often from the second day of the disease, extending throughout the entire illness, and disappearing rapidly with defervescence. Exceptionally. the albumin in the urine has been in considerable quantity, precipitating by the heat and acid test, but rarely containing renal elements in the shape of casts or epithelium. The early appearance of albumin in dengue, when present, might be considered a differential sign, between this disease and yellow fever, apart from others, which need not be discussed here. It must be understood that very mild albuminuria has been met with in general; the other condition of actual nephritis serving as the exception to confirm the rule stated. Albuminuria in dengue has not been usually described, but the facts mentioned are certainly true regarding our recent experience. Perhaps, we have been more careful than is customary in the search for abnormal elements in the urine. At any rate, the records at the hospital for infectious diseases (Las Animas), where upwards of seventy cases have been observed, corroborate any statements made.

One more feature of the conditions met with demands our notice. After the first access of four or six days, a short period of a few days elapsed before the second access, or the latter never took place; but in either case patients were frequently left in a state of profound adynamia, extreme mental and nervous depression, which lasted from a few weeks to two or even three months, rendering the convalescents prone to sequelæ of varying degrees of intensity.

There can be no doubt in the minds of those who have closely followed the course of this epidemic that it was an indirect but none the less evident factor in predisposing in favor of other infections; in other words, that an attack of dengue left the individual a fit subject to acquire other severe or even fatal infections. Personally, I saw several cases of grippe, one of dysentery, and one of typhoid fever in persons who, it seems to me, would have better withstood these infections had it not been for a previous attack of dengue fever. Yet, the mortality was low. In a city whose population is estimated at 266,000 inhabitants, we have had but six or eight deaths directly attributable to dengue. One of these patients whom I had occasion to see died of cerebral meningitis, the disease having begun and continued during the first week as a case of dengue; the meningeal symptoms then became marked, and the man died within a fortnight afterwards.

The diagnosis of dengue is not difficult when we know that an epidemic exists in the locality, but I know of no disease which may be so readily mistaken for yellow fever during the first forty-eight or seventy-two hours. The clinical picture (cephalalgia, backache, fever, and sometimes albuminuria), cannot be more like that of yellow fever. We cannot rely on the intensity of the symptoms, for aside from the fact that different individuals appear to have a most varying degree of sensibility, the pains, fever, and other signs do not present themselves at the same period nor in the same way in all cases. Of course, jaundice is not met with in dengue. but we have autopsied a body in which we could appreciate no jaundice during life, and found the lesions of yellow fever. I think Faget's sign is a fairly constant differential index, for in dengue the tendency is for the pulse to correspond with the variation in the degree of temperature, although sometimes we meet a comparatively slow pulse as a result of the generally depressed condition noted. A most careful and painstaking examination of cases can only help to differentiate these diseases. It seems needless to say that when black vomit occurs, dengue can be excluded, but yet some cases of this disease show a slight tendency to bleed from the gums or nose, a fact recognized by all authorities who have made a study of dengue in the various epidemics (Report from Brisbane, *Journal of Tropical Medicine*, December 15, 1905).

When these facts are taken into consideration, can any one wonder that the first cases of yellow fever which occurred in Havana in October, 1905, during the height of the dengue epidemic, passed unnoticed?

THE STUDY OF TROPICAL MEDICINE: ITS AIM, ITS METHOD, AND ITS SCOPE.[1]

BY F. C. WELLMAN.

The remarkable and general interest in the problem of tropical pathology which now exists is of comparatively recent growth. When Dr. (now Sir) Patrick Manson, then a medical missionary in Amoy, China, published his study of *Filaria sanguinis hominis* in 1883, but little scientific knowledge of tropical ailments had been collected. So that it may be truthfully said that Sir Patrick has seen in his own professional lifetime practically the whole development of the great subject to the advancement of which this society is devoted. And this activity has been redoubled within the last few years. The establishment of schools and professorships of tropical medicine in London, Liverpool, Paris, Hamburg, Lisbon, and different parts of the United States, the founding of the *Journal of Tropical Medicine,* the organization of the American Society of Tropical Medicine, the various scientific expeditions sent out from America, England, and Germany for the study of tropical diseases, and the enormous literature dealing with this department of medicine, all emphasize this activity. It is in the hope of possibly increasing the gratifying interests already obtaining in the important subject under review that I have ventured to address you on this occasion.

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[1] A paper read before the American Society of Tropical Medicine, 1905.

Before entering upon the discussion of our topic, a word as to the form in which it has been announced may not be considerd out of place. The term "tropical medicine" has been objected to, and, while a convenient designation, is (it must be confessed) apt to be misleading to those whose interest in and knowledge of the subject is slight. Of course scientific medical men know that there are almost no tropical diseases in the strict interpretation of that term. In short, it is just as allowable to speak of tropical zoölogy or tropical botany as of tropical pathology—really one might almost as well say tropical chemistry. All pathology is one, be it arctic, temperate, or tropical. Still the term has done good. It has been a watchword, it has stood for a fine type of specialization, and it has served well as the expression of a point of view from which various important diseases new and old have taken on a different meaning, the practical outgrowth of which has, in not a few cases, meant the physical betterment of millions of human creatures. As a fortunate result of this the time has now come when no one can claim to be *au courant* with the science of general medicine without an appreciative acquaintance with the leading facts of tropical pathology. So the term can be said to have fully justified its adoption and to deserve well of us.

In speaking of the aim of our Society and the movement it represents, it may be well to premise in the first place two or three statements which can hardly be disputed. These are as follows:

1. The successful settlement of the tropics is of very great importance to the world.

2. Such settlement depends in no small measure on the solution of various hygienic and epidemiological problems there obtaining.

3. In the absence of this knowledge an enormous extra expenditure of lives and money is certain to ensue.

4. The problems in question can best be studied and met by trained observers working at first hand—in other words, by scientific medical men living in the tropics. With these points before us there is no occasion for me to dwell on the necessity for adequately equipped pathologists, clinicians, and sanitarians, specially trained in the lines along which their investigations will run, to take up the enormous task awaiting them. It is little less than a cardinal sin to send a poorly equipped man to the tropics. With the urgent need for exact knowledge concerning the geographical distribution of tropical disease conditions and the factors necessary for their maintenance (upon the possession of which depends such vast issues), and the almost infinite possibilities of tropical hygiene before our minds, I shall leave the further contemplation of our aim as stu-

dents of tropical medicine and pass to my next point.

I can probably discuss methods of study in no more profitable manner than by using as illustrations some of the best work that has been done in the past. The time is too short to admit of detailed examples, but on the subject of animal parasites (of peculiar interest to us) the sound work of a host of men from Cobbold and Leuckart to Blanchard, Stiles, and Braun is ever before us; while on malaria the brilliant researches of Laveran, Manson, Ross, and the Italians (not to mention our own American confrères, from among whom none would omit the names of King and MacCallum) leave almost nothing to be desired. In the science of bacteriology, too, it would be almost invidious to single out for mention any two or three from the splendid army of those who are successfully working along the lines so ably marked out by Pasteur and Koch. All this heritage, together with a goodly amount of purely academical work such as that lately done by Schaudinn and others, has fallen to the direct advantage of tropical medicine. Many excellent special publications in scientific medical journals, too, have added their quota, while such books on tropical diseases as those of Corre, Roux, Davidson, Scheube, Manson, Brault, and Mense point to methods which have resulted in the successful elucidation of many phases of the subject and large additions to the general knowledge of disease. Taking now some special instances: The demonstration of the method by which yellow fever is transmitted, which I have heard referred to (by one than whom our generation has produced no more distinguished exponent of the science of medicine) as "one of the most brilliant and conclusive investigations in the history of pathology," naturally occurs to me. The methods by which this was accomplished are familiar to us all and out of the reach of none. Ross's admirable work in India on the life history of the malarial *Hæmosporidium,* and the classical researches of Smith and Kilbourne on Texas fever, are equally well known. The observations of Castellani and Bruce, Leishman, Dutton, Novy, Rogers, and others on trypanosomiasis in relation to sleeping sickness and kala-azar are models of their kind. The records of these and other equally meritorious achievements are open to us and point the way to further and even more fruitful effort.

Now a concluding word under this head as to the personal equation in the matter. As Sir Patrick Manson (who has well earned the title of Nestor of all tropical workers) has said, "the student of medicine must be a naturalist before he can hope to become a scientific epidemiologist or pathologist or a capable practitioner." Even the inestimable advantage of being on the ground in the midst of fresh material cannot confer the ability to observe accurately. Institutes of research like those, for example, in the Federated Malay States, Manila, and at Khartoum are steps in the right direction and worthy of all praise; but the earnest individual worker need not hastily despair. Granted the capacity for work and achievement, neither complicated apparatus, skilled assistants, nor unreasonable effort are necessary for the study of some of the most pressing problems which tropical pathogenesis is forcing to our notice. Most valuable information concerning some of these questions can be obtained by the expenditure of a little time, care, and patience on the observation of, for instance, the blood parasites of mammals other than man and of the Reptilia found in the torrid zone. In fine, a zeal for the acquisition of knowledge is a *sine qua non* which is well illustrated by the anecdote I once heard of Dr. C. W. Daniels, who was accustomed when in Africa to sit down under a tree, unpack his microscope, and carefully examine the blood of any one of his porters who chanced to fall sick on the march.

I come now to the scope presented by the study under discussion. This is a subject too large for more than a passing mention on this occasion. A few illustrative examples must likewise here suffice. It is not necessary to more than allude in this connection to the very incomplete state of our knowledge of the geographical distribution of disease. The epiphytic skin diseases of the tropics, the behavior of the ordinary bacteria in hot climates, the peculiar form which some cosmopolitan diseases assume in warm countries, all offer fruitful fields for investigation. The generally richer flora and fauna would lead us to expect greater diversity of noxious organisms than in temperate zones. The inexplicable absence of some diseases from the tropics presents no less interesting questions than do some distinctively tropical ailments the etiology of which is as yet shrouded in uncertainty.

Another subject of great moment is that of the intermediate hosts which subserve various parasites. For example, the life history and seasonal prevalence of but comparatively few mosquitoes and other blood-sucking Diptera have been observed. The hemophagous acarines and Rhynchota have never yet been adequately studied from this point of view. If I may be permitted a personal allusion, I might illustrate the foregoing remark by stating that of thirteen species of mosquitoes collected by me in a small district in West Africa, seven proved to be new to science; of eleven different biting-mouthed flies only one had been previously described; and the district was shown to rejoice in several new blood-sucking ticks. The largely systematic work of Theobald and Austen and the valuable bionomical observations of Howard, Giles, and Nuttall have hardly touched this immense and most important subject. On the other hand, not forgetting bacteriology, it may be said that while parasitology (as has been already pointed out) is perhaps the most important branch of tropical pathology, yet it is also the best worked, and the phytoparasites of warm climates offer now perhaps even a more inviting field for research.

In conclusion I can but hint at some special work that should immediately claim our attention. The completion of the investigation of the so-called Leishman-Donovan bodies; explanation of the puzzling dyscrasia in certain obscure fevers; observation of the new Maxwell-MacLean disease; critical examination of the suggested relation between ainhum and leprosy; further confirmation of the work done by Ross and Milne and the Liverpool School on "tick fever," and by Christy and Feldman on the intermediate host of *Filaria perstans;* a study of the quite neglected sarcosporidia and gregarines of the tropics (to say nothing of the special hygienic, surgical, and ophthalmological questions which specialists in hot climates have raised)—all these sufficiently indicate that the scope of tropical medicine is practically unlimited and the work still in its commencement.

MALARIA IN THE TROPICS.*

WILLIAM C. GORGAS, M.D.
Colonel and Assistant Surgeon-General, U. S. Army; Chief Sanitary Officer, Canal Zone.

ISTHMUS OF PANAMA.

Since 1898 I have served almost continuously in the tropics—four years in Cuba and two years at Panama—part of the time with troops, but most of this time being connected with municipal sanitation.

At Santiago, Cuba, I was with the army at the Base Hospital at Siboney, where all the seriously sick were sent during the entire campaign against Santiago until the army returned home.

In Havana I had charge of the yellow-fever wards at Las Animas Hospital. Las Animas was the hospital for contagious diseases for the Sanitary Department of Havana, and, while a large majority of the patients treated by me there had yellow fever, a considerable number of malarial cases were also received, being mistaken for yellow fever.

Here at Panama I am in charge of the yellow-fever ward. All non-immunes with fever from any cause coming into Ancon Hospital are sent to these wards, and much the larger proportion of these cases are malaria. We treat something like two hundred cases of malaria each month in these wards.

I give here my experience in some detail so as to indicate what my opportunities for observing malaria in the tropics have been. This experience has impressed on me the fact that malaria in the tropics is by far the most important disease to which tropical populations are subject, either military or civil. While the percentage of fatalities is not nearly so great as from some other tropical diseases, the amount of incapacity caused by malaria is very much greater than that due to all other diseases combined. I was very much impressed with this at Santiago. While we had more deaths from yellow fever and typhoid fever than from malaria, the latter was the disease that prostrated our splendid little army. About the beginning of August there were very few individuals that were not suffering from fever, and the army, as a whole, was scarcely able to move. The mental depression caused by this general sickness can hardly be appreciated by any one who did not see it, and against a fresh enemy of greatly inferior strength our army at that time would have been entirely helpless. This campaign was a good illustration of what might occur to an army operating in the tropics and subjected to unchecked malaria. I have not at hand the statistics to which I can refer concerning the mortality from malaria during this campaign, but my recollection is that it was not very fatal. I recollect very few cases of pernicious malaria or black-water fever.

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* Read at the Annual Meeting of the American Society of Tropical Medicine, in Philadelphia, March 24, 1906.

In a tropical city like Havana, where I spent the four years succeeding the Santiago campaign, malaria was by no means so general as one would expect. The anopheles have very little opportunity of breeding about a city except in the suburbs, but even at Havana a greater number of persons died from malaria every year than from yellow fever. In Havana all our efforts and attention were given to the eradication of yellow fever, and very little emphasis was laid in our reports on the effect which the mosquito work had on malaria. This, however, was very marked. The average number of deaths reported in Havana from malaria for many years had been about 350; in 1901, our first year of mosquito work, it was 151; in 1902, 77; in 1903, about 50, and it has remained since that date at about 40. I consider that for a city the size of Havana this means the practical extermination of the disease, as that number of cases in the ordinary course of events would be brought in from the outside, or be due to mistakes in diagnosis.

Panama, I suppose, is as favorable a place for the development of malaria as could be found. The towns of Colon and Panama, at the termini of the canal, are not large enough to do away with the breeding of anopheles; that is, anopheles breeding in the suburbs can very well travel to the centers of these towns, and the population living along the canal in little villages a mile or two apart, between Colon and Panama, are ideally situated for the development of malaria. About one-third of the canal runs through a low alluvial and marshy plain, and the other two-thirds pass through a hilly and mountainous country. Along the banks of the little rivulets, which run in every direction, the anopheles breed just about as well as in the marshy level country, and the very general infection of the population by malaria causes most of the anopheles near human habitations to become infected.

We knew from the experience of our predecessors on the Isthmus that malaria would be our greatest trouble, and we did what we could toward correcting the conditions. Our greatest endeavor has been toward draining the localities near all towns and dwellings, so as to make the ground as dry as possible, and in order to leave as few breeding places as possible for the mosquitoes. In places that could not be drained, oil was used very freely.

With a large body of laborers such as we have here, I think an equally important measure is the giving of prophylactic doses of quinin. We also screened as many of the houses as possible and influenced all inhabitants to use mosquito-bars. These measures followed up persistently have had a great effect in reducing the malaria.

With a force of 22,000 men on the pay rolls during February, we had only twenty-two per thousand incapacitated every day on account of sickness. As I said before, fully three-fourths of this sickness was due to malaria, but the total would not be a large sick rate in a healthy locality in the United States. In my wards at Ancon I have personally treated 1,055 cases of malaria in the last six months. In each of these cases a blood examination was made and the character of parasite recorded. The estivo-autumnal variety largely predominated, but the attacks in general were mild and yielded easily to treatment. Among these 1,055 cases we have had only five deaths. So far as personal care for malarial fever is concerned, I believe that the most important thing the individual can do is to take a small dose of quinin daily. While this will not always prevent attacks, in a given body of men it will enormously reduce the number, and I think will prevent a severe type of the disease when it comes. The good results we have had in hemoglobinuric fever have surprised me most. In these wards we have had twenty cases of hemoglobinuric fever in the past eight months, and of these we have lost three.

The treatment has been the persistent use of quinin as soon as we could get hold of the patient. For the first three or four days the quinin is given hypodermically, but as soon as the patient ceases to vomit it is given by mouth; twenty grains in the twenty-four hours hypodermically and thirty by mouth has been the ordinary course. I have seen no evil results that could fairly be attributed to the administration of quinin, and I have often wondered if it could be the same disease which the English have on the west coast of Africa and in which so many of their leading practitioners think that quinin does harm.

The malaria we have here at present among the whites seems to me about as grave, and no graver, than the malaria which I treated in the garrisons along the gulf coast in the United States.

I look forward very hopefully to a diminution in the prevalence of malaria down here. It seems to me that by the continuance of our present measures we ought still further to decrease malaria. Year by year the ditching will decrease the number of anopheles near the habitations along the Canal Zone, and the treatment of the patients in hospital and the constant giving of prophylactic quinin will decrease the number of people who are liable to spread the infection, and I believe that these two forces will act and react as time goes on. Our conditions have been as trying in the past year as they are likely to be. We have had a larger force of men than the French had. The population was very generally infected with malaria, and the ditching and draining had just been completed. All these conditions ought to improve steadily as time goes on, and it seems to me a perfectly rational hope that malaria will decrease in the same ratio. Even if we can not decrease malaria below what it is at present, we will have succeeded in building the canal with no greater number of days lost from disease than if we were building it at home. I hope to do better than this.

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CHICAGO:
PRESS OF THE AMERICAN MEDICAL ASSOCIATION,
ONE HUNDRED AND THREE DEARBORN AVENUE,
1906.

FATAL CASE OF BLACKWATER FEVER SUPERVENING ON AMEBIC DYSENTERY AND SHOWING MALARIAL PARASITES IN THE BLOOD.*

F. CREIGHTON WELLMAN, M.D.

BENGUELLA, WEST AFRICA.

Patient.—Lieutenant M. de G., aged 26, Portuguese, was first seen Dec. 20, 1904.

History.—The patient had been in Africa two years. The first year and a half of this time were spent on the coast, the last six months in the interior. He has never suffered much from malaria nor blackwater fever. Recently he was again sent to the coast, where he spent three weeks. As he was leaving to return to the interior he was attacked with a sharp diarrhea and passed some blood. He recovered in a few days and continued his journey. He has had some looseness of the bowels, with occasional pains, ever since. After his arrival at Bihi fort he had a relapse of the "diarrhea" and was in considerable distress and very weak. He thought he also had some fever, so he came to me for advice.

General Condition.—The patient was thin, weak and feverish. He had no appetite. His tongue was foul. Temperature was 102.4 F., pulse 93, respiration 28. The spleen was slightly enlarged. There was tenderness over the lower bowels. The other organs were normal. At stool there was moderate tenesmus. He had taken no medicine except a diarrhea mixture, ingredients unknown. He considered this the second day of his disease (relapse).

Examination of Feces.—The stools were small and unformed, consisting almost entirely of blood and mucus. There was one moderate-sized slough. Under the microscope many amebæ morphologically identical with *Amœba coli* (Lösch) were seen.

Examination of Blood.—Both fresh and stained specimens were examined, one of each. In the latter two malarial parasites were seen; both were small intracapsular forms. The

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result of a differential leucocyte count was as follows (about 50 cells counted):

Polymorphonuclears	51.5	per cent.
Lymphocytes	26.	per cent.
Large mononuclear	17	per cent.
Transitional	3	per cent.
Eosinophiles	2	per cent.

The initial and succeeding erythrocyte counts are shown in the chart.

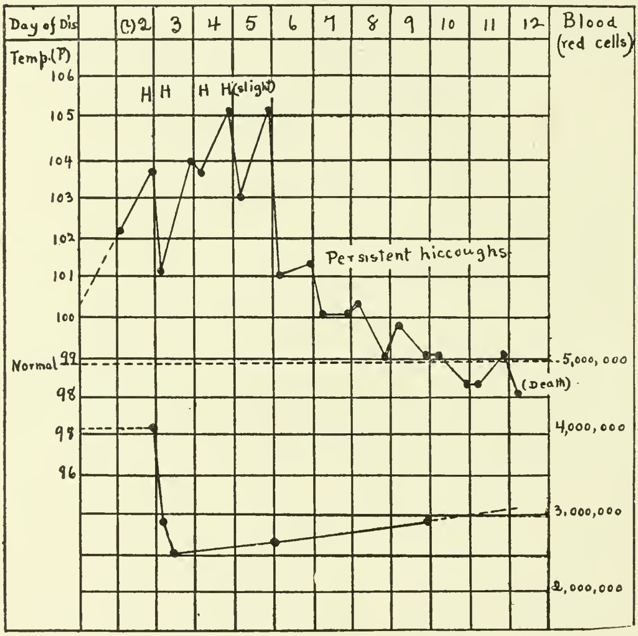

Chart 1.—The blood counts were made on the Thoma-Zeiss hemocytometer. In the first two counts, the blood was also centrifuged and the reading on the hematocrit compared with the result of the actual count. H = hemoglobinuria.

Examination of Urine.—The urine was dark but clear. The spectroscope revealed none of the compounds of hemoglobin. There was a trace of albumin.

Course of the Disease.—The patient was placed in bed (11 a. m.), and small doses of Epsom salts in solution every hour were prescribed. He was placed on liquid diet with a little brandy. In spite of frequent sponging of the body the temperature steadily rose until 5 p. m., when the hemoglobinuria set in.

Re-examination of Urine.—After the hemoglobinuria set in, the urine was re-examined; the color was about like that of porter or stout. There was a dirty-gray sediment, showing under the microscope débris, masses of hemoglobin, and some hyaline and granular casts. The urine was not spectroscoped at first. In later specimens the bands of both oxyhemoglobin and reduced hemoglobin could be seen by shaking up the urine, examining it, adding ammonium sulphid and examining again.

Further Course of the Disease.—*Amœba coli* persisted in the stools (which showed some improvement) throughout the attack, but malarial parasites were not demonstrated in three successive blood examinations. On the morning of the sixth day of the disease the temperature was found to have spontaneously fallen to 101 F. The following day severe hiccoughs set in which nothing availed to control. The patient died at 4:20 p. m. on the twelfth day.

Treatment.—The treatment pursued was entirely symptomatic and expectant. The saline routine for the dysentery, liquid nourishment and stimulants were administered for the weakness and the usual ineffectual gamut of sedatives and other devices were tried to control the hiccoughs. Quinin was not administered at any period of the attack as hemoglobinuria was feared from the first.

REMARKS.

1. This is the thirty-fourth case which I have studied more or less carefully in West Africa. Of this series 29 patients recovered.

2. The case just recorded is the only instance in which death occurred during the first attack. This may be explained by the previous and synchronous dysentery.

3. In three cases malarial parasites were seen in the blood immediately preceding the hemoglobinuria. In the present case the return of the dysentery probably brought about an explosion of latent malaria, and the two conditions combined were able to produce the physiologic depression and hypotonicity of the blood that invited the intercurrent hemoglobinuria.

4. The question of the relation between malaria and blackwater fever is of great interest, but too intricate to be discussed in a paper of this kind. I believe that they are related in some way, and I have shown that in southern Angola the geographical distribution of *Myzomyia funesta*, Giles (the principal carrier of *H. præcox* in West Africa), severe malaria and hemoglobinuric fever closely coincide. The precise character of the relation between the two diseases (which is disputed by some) has not yet been shown.

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BERIBERI ON THE ISTHMUS OF PANAMA.*

IRA A. SHIMER, M.D.
Captain, Assistant Surgeon.
U. S. ARMY.

It is not the purpose of this paper to give any new information on the etiology of beriberi. The subject has been extensively investigated by Pekelharing and Winkler, Manson, Wright and the Japanese school, and germs have been isolated, which, it is claimed, are the cause of the disease. These claims, however, have not been substantiated. Beriberi has been attributed to faulty diet, to various forms of intestinal parasites, to exposure to the elements, and, finally, in absence of definite knowledge, to malaria. The consensus of opinion is that beriberi is a place infection and probably of microbic origin; it is immaterial whether, as Manson states, the germ is located in the soil of infected spots and produces a toxin which gains entrance to the body and causes the symptoms characteristic of the disease, or whether the germ itself gains access to the body and there generates a toxin which produces the disease.

The knowledge gained by the Japanese during the late war toward the prevention of beriberi by the changed dietary proves little or nothing, because, as pointed out by Scheube, late professor of the Medical School at Tokio, so many hygienic reforms were put into effect at the same time, which by themselves would tend to improve the general health. Beriberi attacks persons living in damp, ill-ventilated and overcrowded buildings; in this locality it has been especially noted that it is common among the pearl fishers. With the knowledge gained during the past few years relative to the transmission of disease by the mosquito, is it not extremely probable that this insect plays an important part in the

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transmission of this disease? To sum up, the causative agent of beriberi has not been determined, nor has the mode of the transmission of the infection been demonstrated.

Beriberi is a specific form of multiple peripheral neuritis, with frequent involvement of the cardiopneumogastric system, the latter manifesting itself by both functional and organic (dilatation of the right side of the heart) disturbances.

TYPES.

The varieties of beriberi on the Isthmus differ in no way from those generally described, namely, 1, the dry, atrophic or paraplegic type; 2, the wet or dropsical type; 3, the mixed forms. It is proposed to give an outline of the symptoms of each of these varieties.

1. The Dry, Atrophic or Paraplegic Type.—Probably the earliest symptoms of beriberi cases is the pain felt in the epigastrium. This is often present for several months before other symptoms appear. The patient first notices a gradual loss of power in the legs, followed by atrophy of the calves of the legs, with loss of sensation over the front of the tibiæ, the sides of the thighs, and very frequently of the finger tips and of areas on the arms. Manipulation of the muscles is painful. Patellar reflex and ankle clonus are usually absent. The gait in these cases is ataxic; there is marked toe-drop, causing the patient when walking to raise the foot a considerable distance above the ground and to bring it down with a characteristic flop. These patients use various sorts of devices to assist themselves in progression, and when walking with a support place as much of their weight as possible on this support. Examination of the cardiac area shows a greater or lesser degree of pericardial effusion; the heart sounds overlap each other; there is a general cardiac irritability; throbbing of the carotids and pulsating movements in the jugular vein.

2. The Wet or Dropsical Type.—In appearance this type differs entirely from the preceding. The face of the patient is puffy and heavy; the lips cyanosed, and the trunk and members of the body are edematous. The urine is scanty and dark colored, of high specific gravity, but in the majority of uncomplicated cases contains no albumin. The edema is firmer than that of nephritis. It may be localized and disappear from day to day. Hydrothorax and hydroperitoneum are frequently present. There is rarely any edema of the scrotum. The heart shows the same conditions as in the atrophic cases. The patellar reflexes are absent and the disturbances of sensation are the same as in the atrophic cases.

3. The Mixed Types.—In this type of case there is some edema, especially of the feet, about the flanks, over the buttocks and sternum and in the region of the neck. The patellar reflexes are absent; there are areas of anesthesia over the tibiæ. The cardiac symptoms are the same as in the types described above. The general health of these patients is not affected. The appetite is good; the tongue clean, and unless there are complications there is no fever.

SYMPTOMATOLOGY.

In reviewing the symptoms of beriberi, the paralyses and atrophy of the voluntary muscles do not play an important part as to the life of the patient. The real danger depends on the amount of involvement of the cardiopneumogastric innervation. Patients who are up and around one day and apparently doing well suddenly collapse and are dead the following day. This is pointed out by Manson as probably due to a chain of circumstances; to degeneration of the heart muscle following nerve destruction; to imperfect systole in consequence of an interrupted nerve supply and to obstruction to capillary circulation in consequence of vasomotor paresis in the pulmonary and in the general circulation. When the dilatation once begins, it tends to increase of its own accord; the more the heart dilates the more difficult it is for it to contract. Finally, the distension is so great that it fails to contract altogether and death is inevitable. Therefore, the prognosis in beriberi should always be guarded, for the case that is apparently mild may suddenly develop serious symptoms.

BERIBERI ON THE ISTHMUS.

The records of physicians who have practiced on the Isthmus for years show that beriberi was unknown here prior to the year 1887. The death registers of the French Canal Company began in January, 1881; those of the city of Panama in November, 1883. There are no records of deaths from beriberi in either of these registers prior to 1887. In that year the canal company imported a number of Chinese and African contract laborers. The first death from beriberi among the canal employés occurred in July, 1887. The first recorded death from beriberi in the city of Panama occurred in December, 1887, five months after the first death among the laborers of the French company. After its first appearance its spread on the Isthmus was rapid, especially among the poorer classes and among the colored races.

The description of beriberi given above refers to the ordinary uncomplicated cases. Almost all the cases which have come under observation in the hospitals on the Isthmus show numerous divergences from the above, due to the multiplicity of complications. A local practitioner of Panama informed me that 450 severe cases of beriberi which he treated began acutely with chills and fever. The fever was of a malarial type and responded promptly to quinin. After the fever subsided and the patients attempted to go about their usual vocations, they showed the typical symptoms of beriberi. As stated above, probably the earliest symptom of beriberi is the epigastric pain. If this is not severe, it would probably not be noticed by the patient unless his attention was afterward called to it by the physician. Hence the opinion prevailing among local practitioners that beriberi is of malarial origin. To illustrate further the complications in beriberics, it is proposed to add a series of cases, taken from the records of Ancon Hospital, giving the clinical histories and pathologic data, and showing beriberi complicated by malarial fever, ankylostomiasis, chronic nephritis of various types and locomotor ataxia.

CASE REPORTS.

Case 1.—G. M., of Martinique, was admitted to Ancon Hospital Jan. 6, 1906. Patient complained of pains in legs and thighs: of burning sensations in the feet; calves of legs were painful on slightest pressure; patellar reflexes were absent. Albumin was noted in the urine January 25. The patient died Jan. 30, 1906, at 4:10 a. m.

Autopsy—Autopsy at 8 a. m. gave the following findings:

Heart: Right heart considerably dilated. Intestinal tract: Mucosa anemic; no indication of hemorrhage; intestine contained round worms, whip worms, and *Ankylostoma americana*. Kidneys: Enlarged, soft and greatly congested. Spleen: Five times normal size; extremely firm; fibrous elements increased; stroma dark brown color; stained smears show estivo-autumnal parasites. Bone marrow: Estivo-autumnal parasites present.

Comparing the clinical with the pathologic data in this case, the former justified the diagnosis of beriberi, the latter the diagnosis of acute parenchymatous nephritis; of ankylostomiasis and of malarial fever, estivo-autumnal.

Case 2.—J. T., Barbadian, was admitted to Ancon Hospital Jan. 22, 1906; died Jan. 22, 1906.

Clinical Diagnosis.—Bronchopneumonia.

Pathologic Notes.—All subcutaneous tissues were edematous. Right pleural cavity contained about 200 c.c. amber colored fluid; pulmonary edema marked; pericardium contained about 150 c.c. straw colored fluid. Heart was acutely dilated. Spleen five times normal size; deeply pigmented stroma, with miliary patches scattered uniformly throughout. Smear showed many pigmented malarial parasites of the estivo-autumnal type. Kidneys acutely congested. Intestinal tract: Ankylostoma and round worms.

Pathologic Diagnosis.—Acute beriberi, estivo-autumnal and malarial fever, and ankylostomiasis.

In this case the clinical symptoms justified the diagnosis of bronchopneumonia; the pathologic, the diagnosis of acute beriberi, malarial fever and ankylostomiasis.

Case 3.—F. H., Panaman, aged 23, was admitted to Ancon Hospital Nov. 14, 1905; died Nov. 15, 1905, 8:30 p. m.

Clinical Notes.—Illness began with pain in stomach and weakness in legs; patient was unable to walk; there was numbness of legs and hands; ankles were swollen; there was tenderness over tibiæ and thighs; abdomen was tender; morning temperature, 98; evening temperature, 100; pulse, 100 to 124; respiration, 24; ankylostoma ova present.

Pathologic Notes.—Left pleural cavity contained 100 c.c. of fluid; pericardium 50 c.c. of fluid. Kidneys were congested. Intestines: In mid-portion of small intestine were many *Uncinaria americana,* both male and female; duodenum, stomach and remainder of intestinal tract normal. Spleen: Small number of pigmented malarial parasites.

This represents an almost uncomplicated case of beriberi of the dropsical type. The evening temperature of this patient was probably due to the ankylostomiasis, as there were no malarial parasites demonstrable in the peripheral circulation.

Case 4.—Ancon Hospital. Patient showed patellar reflexes absent; marked pain in the calves of the legs on pressure; general anasarca.

Pathologic Notes.—Hydropericardium; hydrothorax and chronic nephritis.

Case 5.—W. J., aged 54, Jamaican, on isthmus 20 years, was admitted to Ancon Hospital March 2, 1905; died March 26,

1905. Patient first noticed swelling of feet, which increased rapidly, extending up the legs; there was considerable amount of pain in calves of legs and knees; patient complained of shortness of breath in walking; temperature normal; pulse, 136; respirations, 28 to 36.

Pathologic Notes.—Peritoneal cavity contained about 200 c.c. amber colored fluid; pericardial cavity 60 c.c. amber colored fluid. Kidneys: Right kidney, weight 2 ounces; cortex, 7 m.m.; pyramids pale; capsule stripped with difficulty in places; right kidney as above.

Pathologic Diagnosis.—Chronic diffuse nephritis.

CASE 6.—A. G., Colombian, colored, was admitted to Ancon Hospital Jan. 31, 1905; died Feb. 10, 1905. Illness began one and one-half months prior to admission, with swelling in the feet; there was pain in the muscles of the extremities, difficulty in walking, and dyspnea.

Examination.—Edema of the ankles and feet; apex-beat diffuse; epigastric pulsation with double mitral murmur; pulse 130; great muscular weakness, especially in legs; wasting of calves of legs and thighs; hand grasp weakened; gait ataxic; patient raised legs with difficulty; there was pain on deep pressure of the calves; knee jerk was diminished; there were no anesthetic areas. Urine showed large quantities of albumin; examination of stools showed the presence of ankylostoma.

Diagnosis.—Beriberi and chronic interstitial nephritis.

Pathologic Notes.—Left kidney was very small; capsule adherent in strips; cortex very thin; minute hemorrhage in pelvis; right kidney one-half normal size and same as above. Heart greatly dilated. Stomach, mucosa showed minute pin point hemorrhages; also the first eight inches of duodenum showed marked injection and numerous pin-head elevations, whitish in color. Pin-point hemorrhages were very numerous.

CASE 7.—J. E., aged 46, American, had used alcohol in considerable amounts for a number of years; he denied venereal history. One month ago patient noticed swelling of ankles. This was followed by loss of power in the legs and irritability of the heart when walking rapidly.

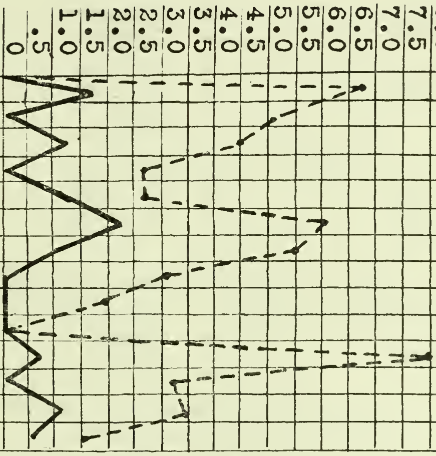
Examination.—Patellar reflexes were absent; ankle clonus was absent; there was pain in calves of legs on pressure; slight anesthesia over tibiæ; Romberg symptom was positive; slight incoördination in movements; Argyle-Robertson symptom was negative.

Cases of this character are very often misleading and it is difficult to make diagnoses between incipient locomotor ataxia and beriberi. It is believed, however, that the absence of the Argyle-Robertson pupil would justify the diagnosis of beriberi, which was made in this case. The subsequent history has confirmed the diagnosis of beriberi.

In autopsies which show symptoms of beriberi and of ankylostomiasis, examination of the intestines very often shows in the duodenum around the worm a large red patch about 4 cm. in diameter. This is superficial and might tend to give one an idea of some pathologic condition due to disease and not to the presence of the worm.

In several deaths from acute beriberi the mucous membrane of the stomach and the upper part of the small intestine was found hyperemic and at some places hemorrhagic. One postmortem showed innumerable white spots, the size of a pinhead, scattered over the mucous surface of the duodenum.

Cases	Deaths	No. of employés	
4	1	7,285	Jan.1905.
4	0	10,000	Feb. "
3	1	9,000	Mar. "
2	0	9,100	Apr. "
2	1	8,700	May "
5	2	10,500	Jun. "
5	1	11,277	Jul. "
3	0	12,000	Aug. "
3	0	19,685	Sep. "
0	0	22,000	Oct. "
15	1	22,000	Nov. "
6	0	22,000	Dec. "
6	2	22,000	Jan.1906.
4	1	23,135	Feb. "



TREATMENT.

As the majority of beriberi cases originate in damp, ill-ventilated and overcrowded habitations, the first essential in the treatment is removal from the probable source of infection. Patients should be placed in a dry locality in well-ventilated rooms. It is customary in Panama to send such patients as can afford the expense to the Island of Taboga. The climate of this island, situated 12 miles from Panama in the Bay of Panama, has long been noted for the beneficial results to patients who have had attacks of beriberi and malarial fever. Patients should be well fed, and bulky articles of diet should be eliminated. The medicinal treatment is entirely symptomatic. Digitalis and strophanthus for the heart, with general tonics and massage and electricity are indicated.

ANALYSIS OF CASES.

In examining the records of cases treated in Isthmian Canal hospitals, 112 cases of beriberi are tabulated. Of this number, 106 patients were males and 6 females. There were 14 deaths among those treated. The admissions to hospital occurred as follows:

1904.		1905.	
September	1	June	9
October	2	July	7
November	0	August	8
December	2	September	5
1905.		October	1
January	7	November	21
February	7	December	14
March	6	1906.	
April	5	January	9
May	4	February	4

Ages at admission ranged as follows:

10 to 20	16	50 to 60	8
20 to 30	45	60 to 70	4
30 to 40	24	Not stated	4
40 to 50	11		

The sources of admission were as follows:

City of Panama and vicinity	77	Pedro Miguel	2
City of Colon and vicinity	14	Gorgona	1
Culebra	9	Paraiso	1
Matachin	2	Bohio	1
Empire	3	Bas Obispo	2

The length of time on the Isthmus outside of the cities of Colon and Panama was as follows:

From Culebra: Five patients had been on the Isthmus upward of ten years. The remaining four had been on the Isthus, respectively, one month, two months, and two about five months each.

The Matachin patients, upward of thirty years.

The Empire patients, five months, one and one-half months and two months.

The Pedro Miguel patients, one seven years, the other four months.

The Bas Obispo patients, one sixteen years and one six months.

The Gorgona, Paraiso and Bohio patients, unknown.

Of the above 112 cases treated in the Isthmian Canal Commission hospitals, 64 patients were employés of the Isthmian Canal Commission. Among these 64 there were 10 deaths. The morbidity was greatest in the month of November, 1905, when with a total of 22,000 laborers there were 15 admissions to hospital, giving a morbidity rate of slightly more than 8 per 1,000 per annum.

The mortality rate among commission employés was greatest in the month of June, 1905. In this month there were 10,500 laborers on the rolls. Five beriberi patients were admitted to the hospital, of whom 2 died, giving a mortality rate of 2.3 per 1,000 per annum. The reader is referred to the chart hereto attached, giving the morbidity rate and death curves for employés of the Isthmian Canal Commission from January, 1905, to February, 1906, inclusive.

In looking over the records of the French Canal Company it is impossible to find the morbidity rate for beriberi. The mortality rate for the French company in November, 1887, was 22½ per 1,000 per annum. Deaths from beriberi were very rare among the employés of the French company during the years 1890, 1891, 1892, 1893, 1894, 1895 and 1896. In 1897, however, the death rate rose to the alarming figures of 54 per 1,000 per annum. This occurred in the month of May. Comparing this with the mortality rate for yellow fever among the employés of the French company, we find that their highest mortality rate from the latter disease was in 1882, and reached 5.8 per 1,000 per annum, or slightly more than 1/10 that of beriberi. To sum up, the highest death rate from beriberi under the Isthmian Canal Commission has been 2.3 per 1,000 per annum, and under the French company 54 per 1,000 per annum.

Deaths from beriberi in the Isthmian Canal Commission by nationality:

Colombia	18	France	2
Dominica	1	Barbadoes	3
Panama	14	Martinique	6
Jamaica	7	Guadaloupe	1
Africa	1	British Honduras	1
Spain	1	Germany	1
St. Lucia	1	Fortune Island	1
Mexico	3		
Costa Rica	1	Total	64
Grenada	1		

Deaths from beriberi in the French company by nationality:

China	65	America	1
Africa	127	England	2
West Indies	25	France	2
Colombia	7	Belgium	1
Cuba	1		
		Total	231

BERIBERI IN THE CITY OF PANAMA.

As stated before, the first death from beriberi in the city of Panama of which there is record occurred in December, 1887. Since that time there has been no year in which there have not been deaths from this cause. For the past 8 years, however, there has been a decided increase in the number of deaths. It is impossible to compare the mortality rate with the morbidity rate, as these cases have heretofore not been reported. The highest mortality rate occurs with great regularity in the last 3 months of each year, namely, October, November and December. Beginning with the year 1899 the mortality rate has risen from 4.5 per 1,000 per annum to 5 in 1900, 7 in 1902 and 11 in 1903. It dropped to 8.5 in 1904 and again rose to 11 per 1,000 per annum in 1905. There were 559 deaths from beriberi reported in Panama from 1887 to 1905, inclusive, distributed by nationality as follows:

China	114	Chile	1
West Indies	36	Venezuela	1
Colombia (Panama)	368	Nicaragua	1
Mexico	9	Cuba	1
Ecuador	5	America	3
Peru	4	France	3
Costa Rica	4	Spain	2
Salvador	3	Italy	1
Guatamela	2	Sweden	1

As an example of place infection of beriberi in Panama, the Bovedas prison may be cited. The ground floor of this building has been used as a prison for many years. It is built of stone, is poorly ventilated and at times overcrowded. The cases originating in this prison by months are as follows:

BERIBERI IN BOVEDAS PRISON.

Year.	Month.	No. of cases.	No. of prisoners.
1904	April	1	Not known.
	May	0	6
	June	0	23
	July	1	31
	August	1	47
	September	2	53
	October	2	58
	November	2	59
	December	2	77
1905	January	0	67
	February	0	63
	March	3	45
	April	0	49
	May	1	51
	June	4	47
	July	3	67
	August	3	68
	September	1	65
	October	3	59
	November	3	56
	December	0	69
1906	January	0	75
	February	0	75
	March	0	69

Late in October, 1905, the prisoners were transferred from the prison proper into another portion of the same building, with conditions practically the same as before. Refernce to the table above shows that after the first month there were no new cases.

The question naturally arises that with the presence of beriberi in Panama, and the appearance of sporadic cases in the Zone, what are the chances of an outbreak of this disease among the laborers of the commission, the same as occurred under the French régime? It is believed that the improved sanitary conditions, better habitations, the feeding of the laborers by the commission, this insuring a better dietary, and our increased knowledge of the management of tropical disease, will all tend to render an outbreak of this disease improbable.[1]

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[1] I am indebted to Dr. Samuel T. Darling, pathologist, Acon Hospital, for valuable pathologic data.

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Reprinted from
THE JOURNAL OF INFECTIOUS DISEASES, Vol. II, No. 4, November, 1905. pp. 627–631

NOTES ON THE COMMON MOSQUITOES OF BIHÉ AND BAILUNDO DISTRICTS, PORTUGUESE WEST AFRICA.*†

FREDERICK CREIGHTON WELLMAN.

THE following notes are based on the collection of *Culicidae* made by the writer in the region occupied by the districts of Bihé and Bailundo, Portuguese West Africa. The collection was begun in 1903, and most of the different species included in it were kindly determined by Mr. F. V. Theobald, of the South-Eastern Agricultural College, England, who is also describing those specimens which are new to science. None of the mosquitoes in this list (with one exception noted in its place) have been reported by other observers from the districts named, and the collection under consideration is the only one which, to the writer's knowledge, has ever been made of the *Culicidae* of this region. The mosquitoes are described in the chronological order in which they stand in the collecting-record. The writer desires to express here his sincere thanks to Mr. Theobald, and also to Mr. Austen, of the Zoölogical Department of the British Museum, whose interest in the distribution and habits of African blood-sucking diptera is well known, and with whom some correspondence regarding the subject of these papers has been carried on.

Culex viridis, Theob.

Theobald. (In letter from Mr. Austen.)

This green, sylvan, "garden" species cannot be mistaken for any other mosquito. I find, however, that it is occasionally confused with a green midge (*Chironomus pulcher*, Wied.) in company with which it is sometimes found. I have been unable to discover where this mosquito breeds, but I suspect that it may be in the small collections of water which are held in the leaves and bracts of large plants during the rainy season. Appears November to December.

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* Received for publication, October 23, 1905.

† Published under the auspices of the American Society of Tropical Medicine.

Myzomyia funesta, Giles.

Theob., *Monograph of the Culicidae*, 1901, 1, p. 178. Giles, *Gnats or Mosquitoes*, 2d ed., 1902, p. 318.

The small size, position of the cross veins, costa with the apex pale, and three pale spots smaller than the intervening basal dark portions, and characteristic wing fringe with pale areas at the end of all the veins except the sixth, together with the banded, white-tipped palpi, black tarsi, thorax, and abdomen, sufficiently mark this mosquito. *M. rhodesiensis* is strikingly like this species, but can be distinguished from it by its unspotted wing fringe and black-tipped palpi.

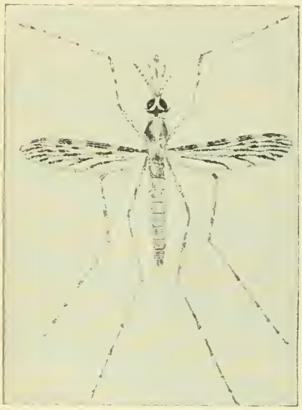
FIG. 1.—*Myzomyia funesta*, Giles. ♀

M. funesta breeds in springs and clear, slow-running water. Very often found in houses. Does not offer to bite much in evening, unless one quietly sits or stands away from the lamp. This mosquito is expert in crawling into small places and often gets under a mosquito curtain. A very common anopheline,[1] and the principal carrier of malaria in this region.

Cellia pharoensis, Theob.

Mono. Culicid., 1901, 1, p, 169. *Gnats or Mosquitoes*, 1902, p. 302.

The characteristic dark gray thorax with two black, eyelike spots is well shown. The tufts at the sides of the abdominal segments, the scaled antennæ, and the large, white spot in front of the transverse wing veins render the species unmistakable. In addition to the fact of its being an anopheline, this mosquito and the following one have a special

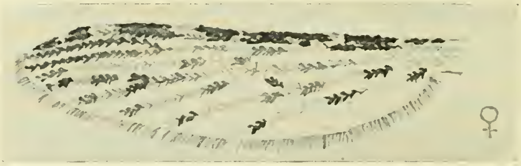

FIG. 2.—Wing of *Cellia pharoensis*, Theob. (After Giles.)

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[1] *Jour. Trop. Med.*, 1904, 7, p. 53.

interest in the light of Low's statement that at least one species of *Cellia* can act as host for *F. nocturna.*

Cellia squamosa, Theob.

Mono. Culicid., 1, p. 167. *Gnats or Mosquitoes*, p. 314.

The somewhat different wing markings and the three conspicuous white longitudinal stripes on the pleuræ easily separate this from the foregoing species. The coal black, densely scaled abdomen with its projecting tufts on the posterior borders of the segments make the mosquito a striking object. It is a rather bold anopheline, and comes readily to a lighted lamp in the evening. Most abundant from November to February.

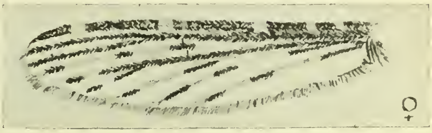

FIG. 3.—Wing of *Cellia squamosa*, Theob.

Anopheles wellcomei, Theob.

Theob. (In letter from Mr. Austen.)

The remarkable size, broad wing markings, and white hind "feet" of this species make it easy to pick out, even without detailed examination of its micro-characteristics. It is generally found near large streams, and I believe that it breeds in running water. A pertinacious biter. Bold even in day time. I find the following note in my diary for June 12, 1905: "Bitten in bright sunlight on the banks of the Cutato River by an *A. wellcomei*, Theob." In shade it will follow one for some distance.

Pyretophorus austeni, Theob.

Entomologist, 1905, 38, p. 102.

This is a new species described from this region. It is a dark mosquito resembling *P. costalis*, Loew, for which I first mistook it,[1] but differs from the type in several particulars, among which the most prominent are the characteristic thoracic ornamentation and wing markings. The dark thorax is clothed with broad, curved, snowy-white scales. Costa with two white spots and a minute third spot near the base. Length, five mm. It is a quiet and unobtrusive, but domestic, mosquito which will breed in fairly muddy pools. It is of interest to point out, in mentioning this mosquito, that the type of the genus *P. costalis* has been proved to carry malaria, and is said to be an intermediate host of *F. bancrofti.* Most abundant in December to March.

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[1] *Jour. Trop. Med.*, *loc. cit.*

Danielsia wellmani, Theob.

Entomologist, 1905, 38, p. 103.

Another new species from this region which Mr. Theobald has done me the honor to name for me. It is a beautiful and distinct species the chief characters of which are its thoracic and abdominal markings and leg banding. The thorax is black with narrow, curved, bronze scales, but with a cream-colored scaled area on either side which expands and meets anteriorly. Abdomen, violet-black with basal, white, lateral spots, becoming median on the last two segments. Legs, dark brown, mid and hind pair with broad, basal, white band to the metatarsi and first tarsi. The description states that the scutellar scales are somewhat broader than in the type of the genus (*D. albolineata*). Length four mm. The ova are brownish and the larvæ are characteristically marked. I hope to publish a study of the life-history at some future time.

FIG. 4.—Head of larva of *D. wellmani*, Theob. (Magnified.)

Culex taeniorhynchoides, Giles.

Jour. Trop. Med., 1904, 7, p. 369.

A new species. The wings are dark and unspotted. Thorax sooty with golden, curved scales and with dense tufts of black scales over the roots of the wings. The black proboscis has a definite ocherous band on the middle. It is a rather large species. Described from a specimen taken in Bihé district, and sent by Dr. A. Y. Massey of Toronto, Canada.

Myzorhynchus umbrosus, Theob.

Mono. Culicid., 1901, 3, p. 89.

This mosquito, determined by Colonel Giles, presents no striking differences from *Anopheles barbirostris*, Wulp[1] or *Mzr. pseudo-barbirostris*, Ludlow.[2] It has, however, but a single costal spot just inside the apex and a very pronounced yellow and black apical fringe. It seems to be a sylvan species. Length five mm.

Mansonia africana, Theob.

Mono. Culicid., 1901, 1, p. 276. *Gnats or Mosquitoes*, 1902, p. 357.

Mansoniae are perhaps the easiest of all the Culicines to determine. Their peculiar brindled appearance and the densely scaled wings with broad, asymmetrical, flat (bracket-shaped) scales on both sides of the veins render them unmistakable. The only genus which they resemble is *Mucidus*, but they lack its characteristic rough "moldy" appearance, and they possess scales of a somewhat different shape.

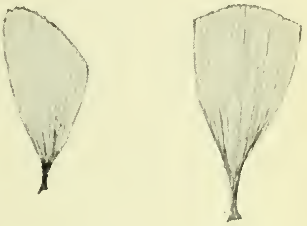

Fig. 5.—Wing scales of (A) *Mansonia* and (B) *Mucidus*, to show difference in shapes. (After Theobald.)

M. africana is distinguished by its thorax, which is ornamented by broad lines of golden-brown and silvery scales and two pale spots. The legs are curiously mottled and banded. Length about four mm. Probably a spreader of filariasis in some regions.

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[1] Leyden Museum *Notes*, 6, p. 48. (Quoted in *Gnats or Mosquitoes*, 1902, p. 308.)

[2] *Jour. N. Y. Entom. Soc.*, 1902, 10, p. 127.

(*To be continued.*)

Reprinted from
THE JOURNAL OF INFECTIOUS DISEASES, Vol. 3, No 2, April 6, 1906, pp. 187-190.

NOTES ON THE COMMON MOSQUITOES OF BIHE AND BAILUNDO DISTRICTS, PORTUGUESE WEST AFRICA.*

FREDK. CREIGHTON WELLMAN.

(*Concluded* from Vol. 2, p. 631.)

Culex hirsutipalpis, Theob.

Mono. Culicid., 1901, 1, p. 378. *Gnats or Mosquitoes*, 2d ed., 1902, p. 403. *Entomologist*, 1905, 38, p. 156.

A LARGE mosquito which has as its striking feature the long, dense, black hairs on the last two joints of the ♂ palpi. It closely resembles *C. plumosis*. Thorax golden brown. Two cream-colored spots on the mesonotum. There is a darkish line down the middle of the thorax. Abdomen dark brown with semi-circular, light-yellow, basal, median, and lateral spots. Proboscis with broad yellow band. Legs brown with cream-colored bands on the tibio-metatarsal and tarsal joints. The wings have the first submarginal cell somewhat longer and narrower than the second posterior. A peculiarity of the wings is the very distinct incrassations (the so-called sixth and eighth veins). The figure of the ♂ ungues in Theobald's monograph is incorrect. He has been able to clear-up this point by dissection of material sent by the writer. The ♂♂ from this region differ from the type in having no pale band at the apex of the palpi, and Mr. Theobald's diagnosis of my first specimen was "*Culex sp. nov.* near *hirsutipalpis*, Theob." The eggs are black and laid in large rafts. A rainy-season mosquito. Breeds in enormous numbers in dirty pools resulting from building, grading, etc. Breeds out readily in captivity. I have kept them for two generations. They vary greatly in size. The type measures 5 mm., but some individuals are a third smaller than this.

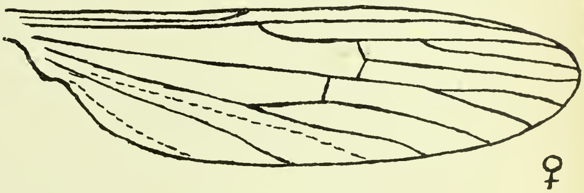

FIG. 6.—Wing Venation of *C. hirsutipalpis* ♀.

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*Received for publication February 5, 1906.

GENERAL REMARKS ON THE GENUS *HEPTAPHLEBOMYIA*, THEOB. AS ILLUSTRATED BY THE WRITER'S SPECIMENS OF *H. SIMPLEX*.

Heptaphlebomyia simplex, Theob.

Mono. Culicid., 1901, 3, p. 337. *Entomologist*, 1905, 38, p. 157.

In view of Mr. Theobald's remark that the fresh "material sent . . . . by Dr. Creighton Wellman has enabled me to add fresh generic characters to those already given," it may be of interest to recall here the main points in his new characterization of the genus. Head clothed with narrow curved scales and upright forked ones except at the sides, where they are small and spatulate. Palpi of ♀ small but prominent, in ♂ acuminate, the last two segments hairy. Thorax, scutellum, and prothorax clothed with narrow, curved scales. In ♀♀ the pleuræ have pointed patches of flat scales, which in the ♂♂ are apically rounded. Wings with typical *Culex* venation, except the seventh long, scaled vein in ♀. In the ♂ there is no true scaled seventh vein, but the sixth is bent at right angles near the edge of the wing. The scaled seventh vein in the ♀ and the characteristic scales on the pleuræ are unique among *Culicidae*.

The species *simplex* (which so far is the only one in the genus) has hitherto been known only from ♀ specimens. The ♂ has now for the first time been described from three individuals collected by the writer. *H. simplex* can, as has been said, easily be told from all other mosquitoes by the ♀ having a distinct, scaled seventh wing vein. It is a remarkable fact that the ♂ does not share this peculiarity. The general facies of *H. simplex* suggests *C. fatigans* while the leg-markings simulate those of *C. creticus*. The thorax and pleuræ are brown, the latter with snowy white dots. The abdomen is dark brown with basal, light, curved bands. There are lateral segmental spots in the ♀, while the ♂ has scattered yellow scales on the apical segment and pale bands on the base and sides of the penultimate segment. The wings in both sexes have the first submarginal cell longer

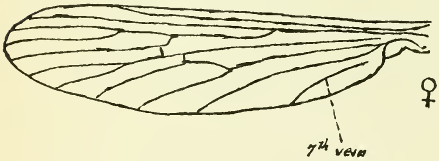

FIG. 7.—Wing Venation of *H. simplex* ♀.

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[1] *Entomologist, loc. cit.*, p. 156.

and narrower than the second posterior. Like the preceding it is a rainy-season mosquito. The eggs are brownish and are laid in rafts. Will breed in foul pools. Length 3.5–4 mm.

SUPPLEMENTARY NOTE ON *MANSONIA AFRICANA*, THEOB. AND *CULEX VIRIDIS*, THEOB.

Cf. *Mono. Culicid.*, 1901, 3, pp. 212 and 273 f.

The mosquito which was determined as *M. africana* (*vide supra*) is not a very common mosquito in the district where I first took it (Bihé), but I have since found it in enormous numbers in a district about a hundred miles from the first named (S. Bailundo), and have had opportunity to compare a suite of specimens with the descriptions of Theobald's *M. uniformis;* and I think with him that they are the same and that the name *M. africana* should sink. Also on re-reading my remark on *C. viridis* I note that my language would convey the impression that the imago is green. The larva and pupa are referred to. The imago itself is brown except the pleuræ, which are greenish gray. I was breeding out larvæ which had been brought me from different sources and all put into one vessel by the collector when I wrote the note mentioned, and the bright green larvæ and pupæ of *C. viridis* were very striking. There is another green larva which sometimes occurs with those of this mosquito. On breeding these out I find they are not *C. pulcher*, as I surmised above, but are a species unfamiliar to me, which I am forwarding for determination. In the course of larva-hunting, since writing the original note on *C. viridis* I have been able to verify my suspicions then stated and find that it breeds in certain *Bromeliaceae*, notably several species of *Amomum* and *Costus.*

It should be borne in mind that the *Culicidae* mentioned in the preceding list are confined to those which are common over the two somewhat extensive districts studied—Bihé and Bailundo. Other mosquitoes, abundant in limited areas, together with a few rare species, will be discussed in a subsequent paper. A full consideration of the pathological significance of these gnats would be of interest but is out of place in a study of this kind. I may say, however, that of the anophelines the most important is *M. funesta*, although I have proven *P. austeni* to be also also a carrier of malaria. I am elsewhere publishing statistics in the form of charts and maps which show the geographical distribution of the former mosquito in this region to be essentially the same as that of severe malaria and black-water fever, and that the amount of rainfall at different seasons of the year has a direct relation, both to the comparative number of anophelines taken and the percentage of malarial infections among the natives.

TROPICAL NEURASTHENIA.*

W. W. KING, M.D.
Passed Assistant Surgeon, Public Health and Marine-Hospital Service.
WASHINGTON, D. C.

Tropical is used here in the sense of locality more than to characterize any special type of neurasthenia. My object primarily is to call attention to its frequency in warm countries, at the same time touching somewhat on the disease as I have observed it.

Writers on tropical diseases make little or no mention of it. Dana, in his work on "Nervous Diseases," states that it is not infrequent in tropical regions and that it is found in the West Indies. My experience extends over six years' residence in Porto Rico, but information derived from various sources has caused me to regard this condition as one quite general to the tropics, differing in degree through peculiar local influences. From what I have been told by medical men who have resided in the Philippine Islands I judge that it is even more prevalent and more severe there than in the West Indies.

The native of the tropics is not exempt, and in Porto Rico, where the percentage of neurotics is high and functional nervous disorders very common, it is not infrequently encountered associated with hysteria—hystero-neurasthenia. It is far more common, however, to find neurasthenics in the tropics among those who go there from colder countries, hence it becomes a very interesting question to American physicians, in view of the close relations recently established between the United States and Porto Rico, Cuba, the Philippines, etc. My remarks refer particularly to Americans living in the tropics, but the same considerations will undoubtedly be found true of other nationalities under like circumstances.

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* Read by title at the annual meeting of the American Society of Tropical Medicine, Philadelphia, March 24, 1906.

Comparatively few individuals entirely escape if they live in the tropics for any length of time. In many persons the manifestations are slight and are taken as a matter of course, due to climate. They do not consider themselves really ill, but commonly explain: "The climate is getting onto my nerves." Acute cases are not unusual. Grave ones are more rare, but do occur, and insanity has been known to follow. Some time ago considerable comment was made in both professional and lay press about the unusual number of American soldiers who became insane while serving in the Philippines. Making due allowance for malingerers who wished to be invalided home, it seems safe to assume that many of these men were victims of grave neurasthenia.

In proportion to the number of American women to men in Porto Rico, I have observed a relative greater frequency among the former. Several explanations may be offered. American women almost invariably menstruate more abundantly than in the States. The flow is prolonged and often so excessive as to require urgent treatment. The interval between periods is usually shortened during the first year or so of residence there. We can readily understand that to women accustomed to a regular monthly routine such conditions may be all sufficient to precipitate nervous exhaustion.

Housekeeping where customs and language are strange and where servants are inefficient and uncleanly has its thousand and one little difficulties and worries that need to be seen to be appreciated, but which in the aggregate are often sufficient to cause housekeeping to be abandoned, the housewife sent to the States to recuperate, and on return to live at a hotel or boarding house.

Another thing: life in most tropical countries is radically different from that in temperate climes. The lack of accustomed society, pleasures and diversions is more keenly felt by women than men, who have more opportunity to make up the deficiency.

Without excluding the usual causes of neurasthenia, there are some which, in my opinion, deserve special mention when considering this as a tropical disease.

Climate is the favorite scapegoat and receives the major portion of the blame. I believe that its influence is overestimated, though it undoubtedly causes a general atony of all the tissues of the body. Functional activity is decidedly lessened. The energetic American goes the pace according to his previous habit, and while his physical and mental capacities may be able to stand it in the States, it is entirely too strenuous for his new environments. He either drops more or less into the pace of the country or breaks down. What may be normal work in one place is overwork in another. Add to this the mental exasperation and irritation which he feels at the slow, easy-going methods of those with whom he comes in contact.

The officials charged with the construction of the Panama Canal have been suddenly confronted with the problem of providing amusement for their employés. They have come to realize that the need is imperative and vital, and are now spending thousands of dollars to meet it. "All work and no play makes Jack a dull boy."

To our notion, the amusements of tropical peoples are limited and often of a character which does not appeal to us. Customs which are not understood and the inability to speak the language make it very difficult to take an active part in whatever opportunities there may be for diversion. Theaters are few and seldom first-class, except in large cities, and here again we meet the impediment of unfamiliar speech. The benefits of public parks and outdoor sports are rarely attainable. Acquaintances are limited to a small circle, the members of which only too often tire of each other's society. In search of something to relieve the monotony of life under such conditions, there is great liability of drifting into alcoholic or sexual excesses, thus further assisting nervous exhaustion.

As to diet, people from the north fare rather badly. The same articles of food (except in a limited number of private houses) appear from day to day with almost clockwork regularity, while the methods of preparation do not result in dishes which appeal to the American palate. The sameness of it all becomes unbearable at times, and a change is sought again and again. The digestive functions, especially that of the liver, become impaired.

Moderate exercise is essential to health in the tropics, but, unfortunately, one's inclination is decidely averse to it. Almost unconsciously everything is done with a minimum of physical exertion. On the other hand, too much or too violent exercise may be more harmful than none at all.

The degree of neurasthenia is slight or moderate, exceptionally, severe. The patient first notices that he is less energetic. He feels fresh in the morning, but soon tires and at night feels worn out, apparently without sufficient cause. He becomes ill-natured, peevish and irritable, taking offense at small things which under ordinary circumstances would not be noticed. Mole-hills become mountains; proper attention can not be given to business; urgent matters are put off from morning till afternoon and from afternoon till next day. It becomes almost impossible to concentrate the thoughts on details or to plan for the future. Memory and the ability to reason may be at fault.

There is a decided tendency toward hypochondriasis, morbid introspection which distorts unimportant pains and ill feelings into supposed initial symptoms of some dreaded disease. The fear of impending disaster or death may render the patient's life miserable, even when he knows that there is no reason for such fear.

The appetite may fail and digestive disorders may arise or grow worse if already present. Loss of weight may result. During a moderate attack I lost about fifty pounds in three months. Sleep is troubled and unrefreshing. Dull, annoying headache is of almost daily occurrence, and, as a rule, is occipital, sometimes frontal if there are visual defects.

True anemia is not a prominent feature, although there is a very deceptive anemic appearance encountered, especially among women who are neurasthenic. I have repeatedly been asked to examine the blood of pale subjects without ever finding any marked reduction of the hemoglobin, unless due to some cause more than the nervous affection. Vasomotor disturbances most probably give rise to this pseudo-anemia.

Neurasthenia in the tropics presents the same great variety of symptoms as elsewhere, and I have only mentioned those which have struck me as specially marked. In slight cases improvement occurs readily or the patient recovers completely when the cause can be removed or its influence counteracted by change of scene or occupation. Proper and regular exercise, particularly if amusement can be combined with it, proves very beneficial, but it is easily overdone.

The symptoms may disappear gradually and the patient recover spontaneously as he becomes more accustomed to his new life and environment; we may say acclimated. The time necessary for this depends on the adaptability of the individual. It may be months or years. Some persons could never do so.

I have had little success with medicinal treatment, unless combined with hygienic measures. Prominent symptoms may require special medication, but the specific medication by drugs designed to act directly on the nervous system will too often prove disappointing.

Reprinted from The Journal of the American Medical Association, May 19, Vol. xlvi, pp. 1578, 1579.

CHICAGO:
PRESS OF THE AMERICAN MEDICAL ASSOCIATION,
ONE HUNDRED AND THREE DEARBORN AVENUE,
1906.

A CRITICISM OF SOME OF THE THEORIES REGARDING THE ETIOLOGY OF GOUNDOU AND AINHUM.*

F. C. WELLMAN, M.D.
BENGUELLA, WEST AFRICA.

My interest in the two rather bizarre tropical affections mentioned in the title of this paper has lately been increased by the opportunity of examining several cases of each disease. In reading over the views commonly held to account for their origin, one is struck by the fact that most of them are purely theories and, like most theories, not free from flaws. A short review of some of these may help to clarify what little knowledge we possess concerning the possible factors giving rise to the obscure conditions known as goundou and ainhum.

GOUNDOU.

SYNONYMS.—*Anakhre* (Agni name), Henpuye (Gold Coast) *Gros nez, Mti* (Zanzibar), Big Nose, Dog Nose, *Uyulue* (Bantu name).

There have been proposed, among others, the following theories to explain the presence of the growths:

1. That they are a sequel of yaws (Chalmers).
2. That the condition is a disease *sui generis* (Braddon).
3. That the condition is an example of atavism referable to some tribal peculiarity of the original negro stock (Strachan).
4. That it is a manifestation of syphilis (Friedrichsen).
5. That the tumors consist of malformations due to non-union of the nasal and frontal bones (Keng).
6. That they are caused by the presence of larvæ of insects in the nostrils (Maclaud).

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* Published under the auspices of the American Society of Tropical Medicine.

The theory that goundou is a sequel of yaws has been put forward by Chalmers, Mell and others. My objections to it may be summarized as follows: (1) The only persons suffering from uyulue (goundou) whom I have seen in Portuguese West Africa (two in number) denied ever having had yaws showed no traces of that disease and were from a district where yaws is almost unknown, a rare imported case being noticed only at long intervals. (2) The symmetrical double growth is against this explanation. (3) Its general geographical distribution does not agree with that of yaws. (4) According to reports, a much larger proportion of men than of women are affected, while in yaws both sexes are affected without distinction.

The second theory that it is a disease *sui generis* is really not an etiologic theory at all, as it attempts no explanation of the symptoms. If by the phrase is meant that goundou is due to a specific micro-organism, it is enough to reply that no such organism has been described.

Strachan's suggestion that the condition may be an instance of atavism is not reasonable in view of the fact that the structure of the tumor, according to those who have studied it most carefully, shows it to be the product of an inflammation. Strachan's observations were made, I believe, in the West Indies, and at least one of his cases was congenital.

The connection of goundou with syphilis is open to most of the objections against its identification with yaws.[1] In my own cases syphilis must be excluded, with the alternative of considering the two cases of goundou (which showed no other symptoms whatever) the only examples of that infection ever seen in an isolated interior bush tribe which I had under observation for several years. Another point is the fact that the coast tribes of southern Angola, among whom syphilis is rife, are no more subject to goundou than the people above mentioned.

The hypothesis advanced by Dr. Keng in the far East that goundou is a congenital malformation due to lack of union of the nasal and frontal bones is founded on the study of one case in which hydrocephalus developed with the tumors. A comparison of his description with my case notes leads me to believe that his case was not goundou at all. The facts that the tumors were soft and pulsating and painful when touched would alone distinguish them from the hard, bony, insensitive growths described by all observers in Africa.

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[1] I do not here enter into the discussion of the identity of yaws and syphilis as maintained by Hutchison, and more recently by Scheube in his "Die venerischen Krankheiten in der warmen Länder," p. 51. For the purposes of this paper the clinical manifestations as seen in typical cases quite suffice.

Maclaud's original idea that the process is, in the first instance, set up by the presence of dipterous larvæ in the nostrils has not been confirmed by the researches of later observers. Manson points out, too, that the symmetry of the growths is difficult to account for on this hypothesis.

It will be seen by this rapid résumé of ideas regarding the cause of the peculiar affection under consideration that none of the explanations proposed rest on anything more definite than conjecture. The tumors are doubtless a hyperplasia, probably due to an osteoplastic periostitis with a very definite cause which, however, has not yet been demonstrated.

AINHUM.

SYNONYMS.—*Guduram* (W. Africa) *Quijila* (Brazil), *Banko-Keréndê* (Soudan) *Sukha-pakla* (*India*) *Exérèse spontanée, Esola, Ombanja* (Bantu names).

I shall consider in connection with this affection the following etiologic theories:

1. That ainhum is a lesion of leprosy (Zambaco).
2. That it is caused by injuries to the toes (da Silva Lima).
3. That it is due to a trophoneurosis (Scheube).
4. That it is a circumscribed scleroderma (Corre).
5. That it is a congenital spontaneous amputation (Proust).
6. That it is the result of self-mutilation by ligatures, the wearing of toe rings, etc. (Gongora and others).

As to the first hypothesis, I have several times lately seen the suggestion that ainhum may be a manifestation of leprosy. Some of these communications enter into the question with considerable definiteness, and in one instance several cases are cited in which all of the patients are reported to have had leprous parents or relatives and to have evinced signs of leprosy aside from ainhum. All this is, of course, Zambaco Pasha *redivivus.* This observer brought to the study of the question an unusually wide and accurate knowledge of leprosy, but seemed to have acquired a habit of annexing various complaints in order to bring them into line with his specialty. An instance in point is his contention that Morvan's disease in Brittany is only a mild form of leprosy, the virus having become attenuated through the isolation of a comparative old population. The identification of Morvan's disease as a form of syringomyelia did not, however, deter Zambaco from later claiming ainhum, on theoretical grounds alone, as another example of attenuated leprosy. The question which Zambaco proposed to himself may be stated in the words which form the title of his communication to the Academy of Medicine in July, 1896: *"L'ainhum des auteurs, constitue-t-il une entité morbide distincte, ou bien n'est-il qu'une modalité de la léprose?"* and the verdict enunciated was *"L'ainhum des négres. . . est une léprose légère, monosymptomatique, dactylienne podique, c'est-à-dire mutilante des pieds."* Such a conclusion is, of course, permissible from the hypothetical side, but on clinical grounds alone it should be remembered that the ainhum-like constrictions sometimes seen in leprosy nearly always affect the fingers and are always connected with other symptoms of leprosy. One could wish, however, that the question had been approached from the pathologic standpoint. The bacillus of leprosy has been found in every tissue of the human body, except the muscles, and has a special predilection for the skin. It would certainly seem fair, then, to demand a demonstration of this bacillus in at least a few of the cases exploited as *Lepre ainoide.* The fact that the geographical distribution of leprosy and ainhum (to say nothing of the racial distribution of the latter) does not coincide detracts, too, from the force of Zambaco's theory, which later authorities seem to adopt on the strength of his name and in connection with it carefully to shun any reference to *B. lepræ* or other features which may be rigidly tested by scientific methods.

In this region, leprosy is not uncommon, while ainhum is comparatively rare. I have collected three cases, however, concerning which I have recently published a note containing the following observations:

1. In none of these cases is there a leprous lesion demonstrable.
2. In none of these cases is the characteristic facies familiar

to those who are acquainted with negro leprosy present, nor are there any of the other early clinical symptoms of leprosy.

3. In none of the three cases is there a family history of leprosy (I have seen the parents of two of the men and the father and grandfather of the third).

4. Only one of the patients comes from a district in which leprosy is known to exist.

5. In none of the cases can *B. lepræ* be demonstrated in the nasal discharge by Ziel Neelson's method, and in one case in which I had amputated the offending toe no bacilli could be seen in a section of the integument from the constricted portion stained after the same method. The histologic architecture, too, is different from that of leprosy, showing only the familiar fibrosis and atrophy common to all cicatricial tissue.

Consequently, I must agree with de Brun (who reported the case on which Zambaco based his opinion above quoted) that *"l'absence, dans les cas d'ainhum, du bacille de Hansen, semble démontrer qu'il ne s'agit pas d'une manifestation lépreuse."*

The hypothesis originally put forth by da Silva Lima to account for the lesions was that the toes are cut by sharp grasses and the like, and the contracting cicatrix produces the condition as usually described. In opposition to this theory is the fact that the ailment has been noticed in negroes who usually wear shoes. But, as Manson remarks, "unless it could be shown that such individuals had always worn shoes this objection to the explanation offered would not apply." Another objection to da Silva Lima's theory is that the disease does not occur equally in all barefooted races. Even in Africa the geographical distribution is capricious. Again, it is stated that in Brazil ainhum is becoming less common among the negroes who nevertheless go barefooted as in former days.

Scheube's suggestion that the lesions are the result of a trophoneurosis makes no attempt to explain the origin of the condition. Such a theory is in the nature of a *tertium quid,* and only puts the difficulty one step farther back.

The view of Corre and Despetits that ainhum is a circumscribed scleroderma is open to the same criticism. Scleroderma is an induration of the skin largely due to hyperplasia of the connective tissue and muscle fibers of the corium. Its etiology is not known, although it has been connected with disease of the thyroid gland. It has also been described as following acute diseases and exposure. The local nature of the lesion in ainhum does not accord well with these views. The thyroid glands in the three patients I examined were apparently normal.

An idea advocated by some (principally by Proust) is that we have to do with amputations which come about by constrictions of amniotic filaments during fetal life. Scheube well urges against this view the facts that such amputations "are congenital and occur on various parts of the body; they are not limited to the toes, are generally multiple and frequently occur simultaneously with other deformities; they, therefore, differ essentially from ainhum."

The wearing of rings on the toes can hardly be seriously entertained as a cause. In the first place, one never sees or reads of rings worn by African natives on the little toes alone. Again, few tribes wear rings on the toes at all, and if the wearing of rings caused the affection the hands would be affected oftener than the feet. The statement that ainhum is self-mutilation through tying strings lightly around the toes is groundless and has not been confirmed.

In conclusion, the above review teaches us that no definite and undisputed cause for the lesion has been advanced. I think that there is most to be said in favor of da Silva Lima's theory. Manson puts the case to the best advantage when he suggests that the condition "is provoked, at all events in the first instance, by wounds so easily inflicted on bare feet in walking through grass or jungle. The fold of skin in which the lesion of ainhum commences is very liable, especially in the splayed-out toes of the negro, to be wounded in this way. If we examine the under surface of the joint flexures of the toes in many individuals of this race, even in those not affected with ainhum, we often find the skin, particularly at the proximal joint of the little toe, thick, rough, scaling and sometimes even ulcerated. One can understand that continual irritation of this sort, produced and kept up by wounds from sharp grasses, would in time give rise, especially in the dark-skinned races so prone to keloid, to fibrotic changes in the derma, which might very well end in a sort of linear cicatricial contraction and ultimately in slow atrophying strangulation of the affected member."

I would insist that the groove around the toe in this affection is, both macroscopically and histologically, a cicatrix. A probable factor in the prolonging of the irritations and inflammations set up by wounds and bruises at this point (which I have never seen mentioned by any writer on the subject) is the chigger, S. *penetrans,* which seems to have a predilection for this particular spot, especially if, as is so often the case, the skin be cut or torn. As to the fatty and atrophic changes in the amputated toe I use the words of McFarland, that their "true cause is not determined; it may be trophic or it may depend on local cicatricial formations."

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NOTES ON THE VITAL STATISTICS OF THE PHILIPPINE CENSUS OF 1903.

BY

ISAAC W. BREWER, M.D.,
of Ft. Huachua, Ariz.

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NOTES ON THE VITAL STATISTICS OF THE PHILIPPINE CENSUS OF 1903.[1]

BY

ISAAC W. BREWER, M.D.,
of Ft. Huachua, Ariz.

The Philippine Archipelago in latitude extends from N. 4° 40′ to N. 31° 10′, and in longitude from E. 116° 40′ to E. 126° 34′. There are 3,114 known islands comprising a land area of 115,026 square miles.

The inhabitants are mostly Malays, Chinese, and Negretos and a mixture of the races. The Negretos, living in the more inaccessible parts of the mountains, are said to number 23,000.

According to the census innumeration there were on March 2, 1903, 7,635,426 people on the islands, 6,987,688 were classed as civilized or partly civilized. There were 8,135 Americans, 6,136 other whites and 41,035 Chinese.

The density of the population for the entire archipelago was 67 per square mile. The most densely populated province, Ilocos Sur, had 398 persons to each square mile; 65 percent of the Christian population (civilized natives) live on the seacoast.

The average birthrate computed from records for the years 1876 and 1885 to 1898 was 47.9 per thousand. The average deathrate for the same period was 39.7 per thousand, but omitting the cholera years 1879, 1889 and 1890 it was 31.7.

The following tables with slight modification are taken from volumes I and III of the census of the Philippine Islands, 1903.

The census was taken under the direction of General J. P. Sanger, U. S. A., Major Charles

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[1] Abstracted for the American Society of Tropical Medicine; published under the auspices of the Society.

Lynch, Surgeon, U. S. A., being his medical adviser.

From a study of the following tables which accounts for 93.9 percent of the deaths in the Philippine Islands and for 65.4 percent of the deaths in the United States, it will be seen that in general the excess in deathrate in the Philippines occurs among the preventable diseases. For such diseases as pneumonia, measles, influenza, typhoid fever, and diseases of the kidneys, the Philippine deathrate is much lower than in the United States. This would seem to indicate that the deathrate in the Philippines will not be excessive when proper sanitary measures have been instituted and when the inhabitants reach such a stage of civilization that they will observe the ordinary rules of personal hygiene.

The mortality among children under five, is very high, being 462 for the brown, 356 for the yellow and 586 for white people. This mortality is largely preventable. Among the native people many children die of convulsions; probably most of them are cases of tetanus, the infection taking place through the cord.

DISTRIBUTION OF DEATHS IN THE PHILIPPINE ISLANDS AND THE UNITED STATES, BY PRINCIPAL CAUSES, EXPRESSED IN PERCENTAGE OF THE TOTAL NUMBER OF DEATHS.—1902.

Cause of death.	Philippine Islands.	United States.
Cholera	31.1	....
Malarial fever	26.8	1.4
Tuberculosis of the lungs	6.6	10.7
Epilepsy	5.1	0.3
Dysentery	3.7	1.1
Convulsions	3.6	1.5
Smallpox	3.4	0.3
Diarrheal diseases	3.2	3.3
Beriberi	1.3	....
Diseases of the stomach	1.2	1.3
Bronchitis	0.7	1.9
Accident	0.7	....

Pregnancy	0.7	0.6
Measles	0.6	1.2
Tetanus	0.6	0.2
Influenza	0.4	1.6
Typhoid fever	0.4	3.4
Diphtheria	0.3	1.6
Croup	0.3	1.2
Asthma	0.3	0.3
Simple meningitis	0.2	1.2
Congestion, hemorrhage, and softening of the brain	0.2	....
Congenital debility and malformations	0.2	....
Erysipelas	0.2	0.3
Tumors	0.2	0.3
Rheumatism	0.2	0.5
Anemia	0.2	0.2
Scarlet fever	0.1	0.6
Whoopingcough	0.1	0.9
Dengue	0.1	....
Other forms of tuberculosis	0.1	....
Cancer	0.1	2.8
Organic diseases of heart	0.1	6.7
Pneumonia	0.1	10.2
Nephritis and Bright's disease	0.1	3.5
Puerperal septicemia	0.1	0.3
Female diseases of the genital organs	0.1	0.3
Paralysis	0.1	2.3
Diseases of pharynx	0.1	....
Diseases of bones	0.1	0.1
Hemorrhage	0.1	....
Senile debility	0.1	2.8
Bubonic plague[1]	....	....
Leprosy[1]	....	....
Suicide[1]	....	0.5

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[1] Represented.

Table I shows the percentages of deaths from the more important diseases by season for the year 1902:

The foregoing statistics confirm the general impression gained from three years' service in the Philippines, that the greatest deathrate occurred in the wet season. Variola is more

TABLE I.

Disease.	Cool Season.	Warm Season.	Wet Season.
Cholera	12.7	15.1	72.2
Beriberi	27.5	33.1	39.4
Variola	28.6	47.1	24.3
Tuberculosis of lungs	29.4	33.0	37.6
Bronchitis	27.2	35.1	37.7
Dysentery	18.3	27.5	54.2
Diarrhea	21.5	29.1	49.4
Malarial fever	34.4	33.9	31.7

TABLE II.

Cool Season			Warm Season			Wet Season		
Month	No. of deaths	%	Month	No. of deaths	%	Month	No. of deaths	%
November	31.022	7.0	March	25,663	5.8	July	54 974	12.4
December	29,631	6.7	April	28,279	6.4	August	54,171	12.3
January	33,906	5.4	May	31,713	7.2	September	54,442	12.3
February	23,742	5.4	June	39,549	9.0	October	44,725	10.1
Total	108,301	24.5	Total	125,204	28.4	Total	208,312	47.1
Unknown, 241								

fatal during the dry season while there is little seasonal differences for malaria.

Table of deaths in 1902 arranged by months and seasons, with percentages of total number of deaths which occurred in each: are shown in Table II.

Table III shows the normal meteorologic conditions at Manila (latitude N. 14° 35′, longitude E. 121°) and the conditions that prevailed in 1902:

The following table of comparative deathrates of whites in the Philippine Islands and the registration area of the United States shows the relatively great mortality among children under five:

Age Group.	Philippine Islands.	United States.
Under 1 year..............	448	165
Under 5 years..............	138	52
5 to 14 years..............	22	4
15 to 24 years..............	20	6
25 to 34 years..............	21	9
35 to 44 years..............	27	12
45 to 64 years..............	47	22
65 and over................	391	87

The deathrates are analyzed by color and those of the brown people by sex in Table IV.

Table V show each of the three most prominent races—brown, white and yellow—and for the eight principal diseases, the proportional number of victims of each disease to the total number of deaths of the race in 1902.

The following table shows the relation of disease to the seacoast:

Disease	Deathrate	
	Interior	Coast
Malarial fever.............	23.7	13.8
Cholera	21.4	18.9
Tuberculosis of the lungs....	5.7	3.4
Diarrheal diseases..........	5.7	3.6
Smallpox	2.2	2.1
Beriberi..................	0.6	0.9

TABLE III.

	Cold Season		Hot Season		Wet Season	
	Normal	1901–2	Normal	1902	Normal	1902
Mean temperature	77·7	75·4	82.2	82.8	80.6	80.4
Maximum temperature	95·9	91·4	100	97·0	95·8	93·9
Minimum temperature	60.3	60.3	63.3	72.1	68.9	71.8
Mean relative humidity	78.7	79·0	75·2	73·9	84.4	84.6
Precipitation	78.87	13·23	15·70	14.86	50.89	46.42
Number of rainy days	28	42	31	40	77	81

TABLE IV.

Age Group	Brown			Yellow	White
	Total	Male	Female		
Under 1 year	321	348	293	—	448
Under 5 years	141	151	131	356	138
5 to 14 years	43	45	41	87	22
15 to 24 years	33	33	33	18	20
25 to 34 years	42	42	42	22	21
35 to 44 years	49	50	48	29	27
45 to 64 years	70	75	65	52	47
65 and over	146	150	142	212	391

TABLE V.

Disease.	Brown.	White.	Yellow.
Cholera	31.1	42.9	31.4
Malarial fever	26.9	4.0	10.7
Tuberculosis of the lungs	6.6	3.3	12.5
Dysentery	3.7	6.0	4.7
Diarrhea	3.1	3.3	2.8
Senile debility	1.5	1.1	0.6
Beriberi	1.3	....	8.3
Diseases of the stomach	1.2	1.6	0.9

TABLE VI.

	Total	Brown	Mixed	Yellow	White	Black	Total per 100,000
Insane	15,372	15,328	16	15	9	4	220
Blind	15,811	15,772	19	13	7	0	226
Deaf	23,227	23,176	16	20	12	3	332
Deaf and dumb	5,910	5,907	3	0	0	0	85

The table should not be interpreted to mean that the lowlands are more healthy than the higher ground. Very little of the higher ground in the Philippines is occupied by civilized population.

Cholera appeared in Manila in March, 1902, and spread rapidly over the islands, causing 31.1 percent of the deaths that year and 19 percent of the deaths in 1903. The total number of deaths from this disease recorded in the census reports was 200,348. During the epidemic of 1879 there were about 400,000 deaths from cholera and in 1889-1890 the mortality from the disease was about 260,000. At the date of the present writing (September 6, 1905) the daily press reports the reappearance of the disease in Manila.

Table VI shows the statistics relative to the defective classes among the civilized population:

Manila, the chief city of the archipelago, is situated on the west coast of the island of Luzon in latitude N. 14° 35′. It occupies the delta of the Pasig river and the soil is damp and badly polluted.

The population as given by the census was 219,928. The deathrates since 1900 were as follows: 1900, 44.5; 1901, 42.6; 1902, 69.2; 1903, 44.7.

The high rate for 1902 was caused by the epidemic of cholera that prevailed during that year.

The following shows the deathrate for Manila and several other tropical cities: Bombay, India, 1901, deathrate 76.7; Manila, P. I., 1903, deathrate 44.7; Alexandria, Egypt, 1901, deathrate 37.3; Calcutta, India, 1903, deathrate 37.0; Cairo, Egypt, 1901, deathrate 34.8; Havana, Cuba, 1901, deathrate 22.1.

In the following table are shown the deathrates for the principal diseases for Manila and the rest of the archipelago for 1902:

Disease	Deathrate for Manila	Deathrate for Archipelago
Convulsions	16.7	2.3
Cholera	15.6	20.0
Tuberculosis of lungs	4.5	4.0
Bronchitis	3.8	0.4
Diarrhea	3.2	2.0
Dysentery	1.9	2.0
Meningitis	1.7	0.2
Malarial fever	1.5	17.0
Beriberi	3.8	1.0

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SOME MEDICINAL PLANTS OF ANGOLA, WITH OBSERVATIONS ON THEIR USE BY NATIVES OF THE PROVINCE.

BY

F. CREIGHTON WELLMAN, M.D.,

of Angola, Africa.

(Published under the auspices of the American Society of Tropical Medicine.)

The study of the plant life of Angola must remain forever linked with the name of Friedrich Welwitsch, whose discovery of that extraordinary plant *Welwitschia mirabilis*, Hook. fil., has made his name familiar to every botanist and over whose tomb have been placed the just words: "*Floræ Angolensis investigatorum princeps.*"

Dr. Welwitsch mentioned and described a number of medicinal plants in his published and manuscript writings, but having slight acquaintance with the different Bantu dialects of Angola, his notes on the native names and medical uses of the same are frequently vague and contain erroneous statements. Examples might be cited of Bantu names of plants with meanings such as "grass," "small grass," "tree from the water," "twig from the jungle," etc., and such mistakes have been perpetuated by writers following him.

In the intervals of some pathologic studies undertaken in the colony in question in 1896, 1899, and 1903, I have been able to identify a few species commonly used by the natives for medicines and to collect trustworthy information regarding the manner in which they are applied. All mention, however interesting, of plants other than those commonly employed as native remedies has been excluded. The plants used in treatment consisting of fetish rites only, have likewise been omitted. It must also be borne in mind that these notes apply to the bush natives of Bihé, Bailundo, and Andulo, with their contiguous tribes, and do not include the half-civilized coast blacks. This study does not pretend, therefore, to be part of an academic discussion of Angolan flora, for which I have neither the requisite leisure nor experience, and consequently I have omitted descriptions of the plants which may be easily looked up in Oliver's "Flora" or in Bentham and Hooker.

It need hardly be pointed out that many of the substances imagined by the Bantus to possess therapeutic value are of feeble effect or inert; yet as the object of this paper is not to set forth what the natives might use as medicines but to state what they do use, I have thought it best to make the list as complete as possible. I have grouped the plants under their natural orders. The vulgar names (without which such a study is useless and can neither be added to nor criticized) are in the Umbundu dialect, the language of the Bihéans, Bailundos, and Andulos, with their allied tribes, and have been obtained at the expense of some time and trouble. I append a short bibliography, which will be useful to any one who may be further interested in the subject.

PHANEROGAMIA, DICOTYLEDONS, RANUNCULÁCEÆ.

Utendulu, *Clematis villosa* var. *scabiosifolia*, De C. The roots are boiled, mashed up, and applied to the skin as a remedy for "Onjuaya," a term which literally signifies itching, and refers to cutaneous pruritus from almost any cause.

ANONACEÆ.

Olumepe, *Monodora angolensis*, Welw. Fruit eaten for pains in the bowels. Sometimes boiled and its juice drunk for the same purpose.

BERBERIDACEÆ.

Okañauñau, *Podophyllum sp.* Roots eaten raw in the treatment of dysentery.

NYMPHACEÆ.

Evonge, *Brasenia peltata*, Pursh. The whole plant is pounded up and applied raw as a poultice in neuralgic pains and in paralyses.

POLYGALACEÆ.

Utata, *Securidaca longipedunculata*, Fres. A weak infusion of the rootlets is used to cure "olosinga," a somewhat indefinite term which indicates pains in the chest, shoulders, etc. The inner bark of the root contains an active poison which is one of the ingredients of the poison test as employed in Angola. Four gm. of this bark boiled in 30 cc. of water and given to a large female mandril (*Cynocephalus sp.*) produced death in 48 minutes. The roots hashed up are used by native women to commit suicide. The method, as described by them, consists in placing small quantities in the nostrils, ears, armpits, and vagina; but in the one case

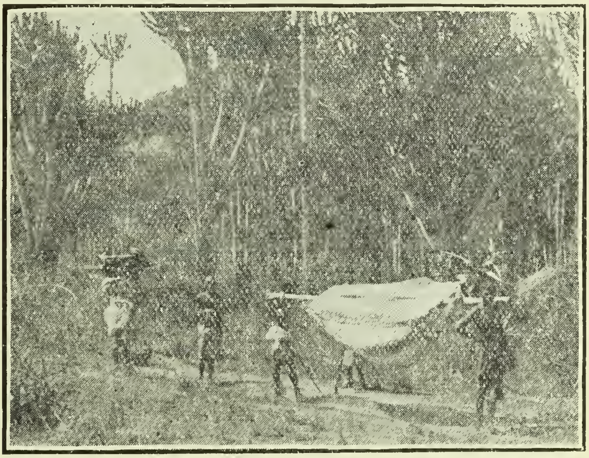

Fig. 1.—Scene in southern Angola showing *Candelabra Euphorbias.*

which fell under my notice an emetic brought up generous quantities of the drug from the stomach. The roots when cut or bruised give off a strong odor of *Oleum gaultheriæ.*

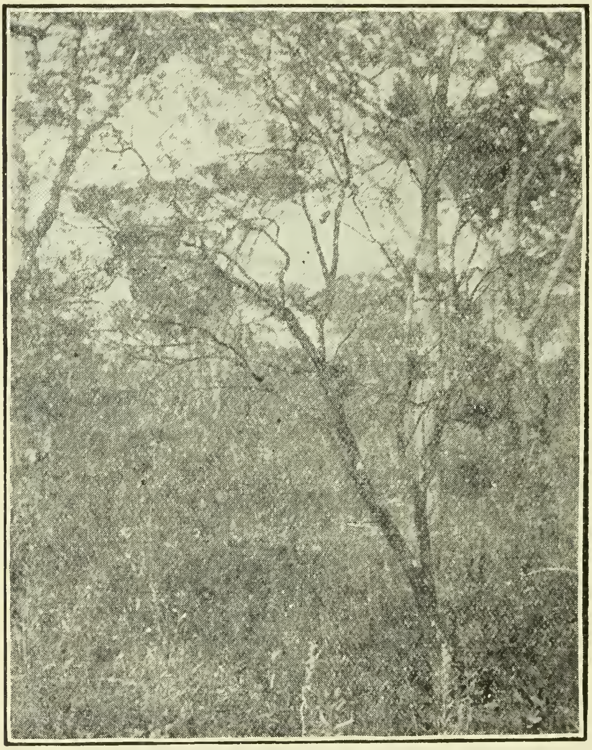

Fig. 2.—*Tamarix articulata*, Vahl.

TAMARISCINEÆ.

Oluvili, *Tamarix articulata*, Vahl. Twigs pounded up raw and applied locally as a remedy for scabies.

MALVACEÆ.

Ocingombo, *Hibiscus esculentus*, L. The mucilaginous juice of the half-ripe pods is dissolved in water by gentle heat and drunk as a demulcent in coughs.

Ukua, *Adansonia digitata*, Juss. This tree is usually found just outside the district in which I made this study, but as the natives procure and use its fruit, etc., I include it here. A decoction of the seeds is drunk after fevers as a tonic stimulant. The pulp of the fruit is also eaten raw to cure diarrhea.

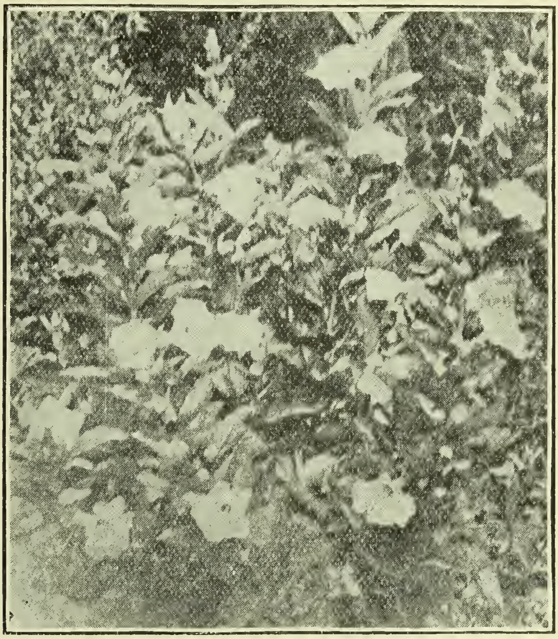

Fig. 3.—West African *Malvaceæ* growing in a swamp.

Utele, *Gossypium sp.* Smoke of leaves inhaled as a remedy for headache. The leaves are also dried by the fire and the odor inhaled for coryza.

STERCULIACEÆ.

Ocitutu, *Xeropetalum cuanzensis*, Welw. In case of childbirth with retained placenta the vulva is bathed with a decoction of the leaves. It is also thought to be good in cases of edema of the external genitals.

BURSERACEÆ.

Umbafu, *Caranarium edule*, Hook. f. The habitat of this tree, like *A. digitata*, lies, strictly speaking, without the region under consideration, but since the products of the tree are used by the natives I have observed, I include the following note. The resin is applied as a balsam to sores and ulcers, and its inhaled perfume is said to relieve headache and accelerate difficult childbirth. The oil is esteemed as an application for strains and bruises. The powdered bark is also sometimes used in the treatment of ulcers. The seeds are often worn round the neck as charms.

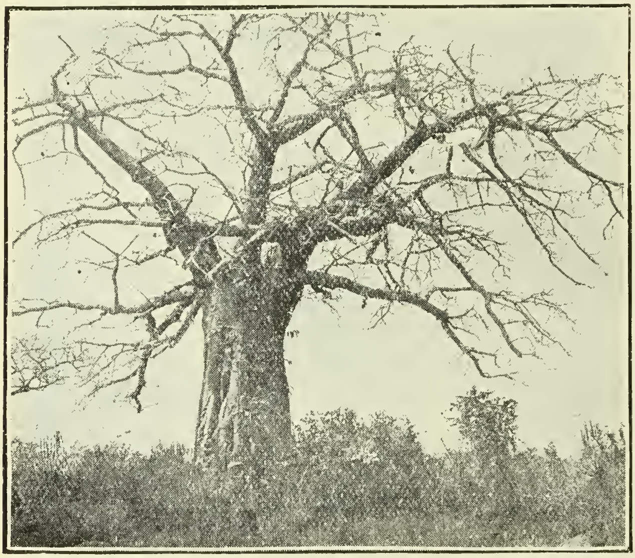

Fig. 4.—*Adansonia digitata*, Juss.

DODONACEÆ.

Utola, *Ptaeroxylon utile*, E. et Z. Leaves chewed up and placed around joints to relieve malarial pains. Bark scraped fine and applied in the same way.

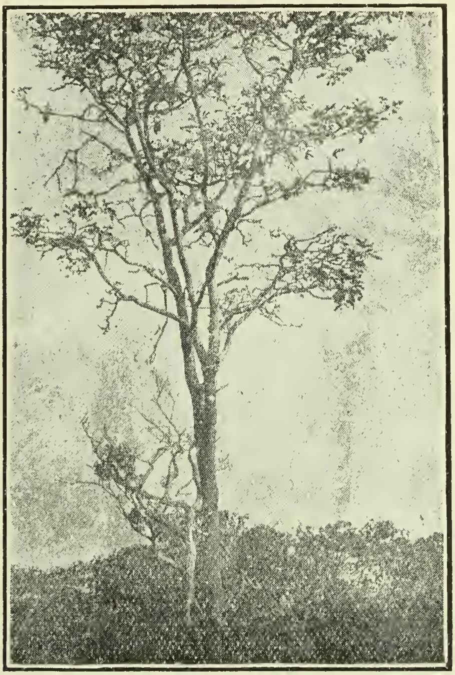

Fig. 5.—*Pterocarpus erinaceus*, Poir.

ANACARDIACEÆ.

Ohumbi, *Odina acida*, Welw. Bark pounded up, boiled, and applied to freshly made wounds.

Usondanduva, *Pseudospondias microcarpa*, Engl. Powdered bark snuffed up the nostrils in case of epistaxis.

LEGUMINOSÆ.

Onjilasonde, *Pterocarpus erinaceus*, Poir. In case of neuralgias and muscular pains, the skin is scarified and the inner bark of the tree hashed up and boiled is applied. The bark is very astringent and is used by the Boers for tanning leather. The gum which exudes when the tree is cut into, closely resembles the gum kino of commerce.

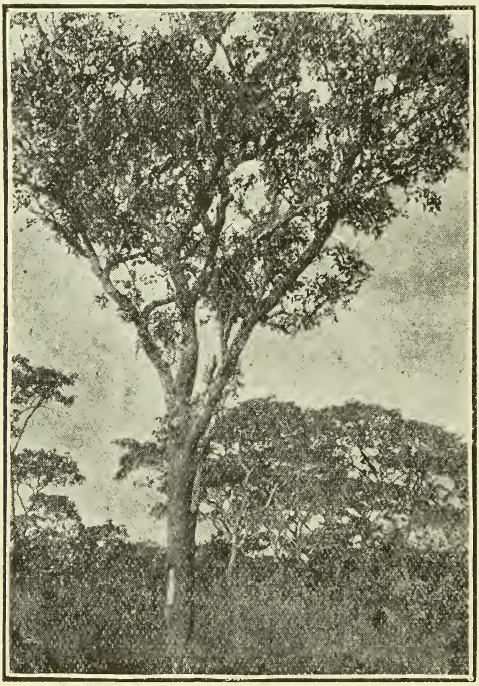

Fig. 6.—*Berlinia paniculata*, Benth.

Ohula, *P. tinctorius*, Welw. Juice of bark given to babies who refuse to eat when being weaned.

Omanda, *Berlinia paniculata*, Benth. Steam from infusion of bark used, along with various fetish ceremonies, in the treatment of nervous disorders.

Omue, *B. angolensis*, Welw. The bark is pounded up, boiled, and the mess taken internally for diarrhea.

Okalembe, *Tephrosia vogelii*, Hook. f. An extract of the leaves is used (just in what manner I cannot learn) in the treatment of obscure diseases, accompanied by dropsy. This is the shrub which is used to poison fish in rivers and streams. It is also mixed with food and employed to kill enemies.

Okapilingau, *Burkea africana*, Hook. The bark, macerated in a little water, is inserted by the women in the vagina as an aphrodisiac. Water in which the bark has been soaked is held to be valuable medicine for hematuria from bilharziosis or other cause. Used in different ways, it is a favorite remedy for sexual disorders-

Ombambu, *Erythrophloeum guinense*, Don. The bark is used for some types of heart disease, but I have not been able to get details. This is the tree which furnishes the principal ingredient in the poison test of the negroes throughout tropic Africa. The bark, which in small doses produces vomiting and purging, has been tested physiologically. If powdered and inhaled it causes sneezing. The aqueous extract when injected under the skin of animals produces vomiting, irritates, and finally paralyzes the vagus nerve, causing the heart to slow, and, in larger doses, to stop. The limbs seem to

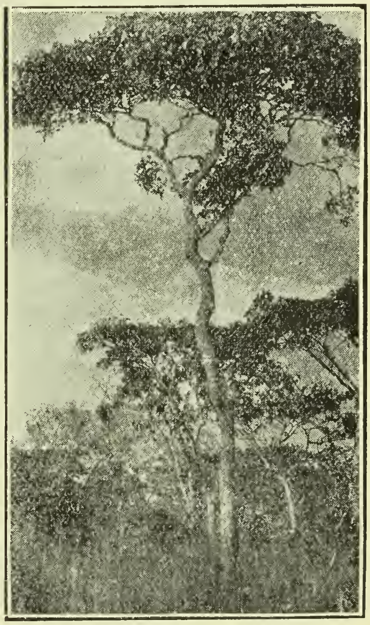

Fig. 7.—*Berlinia angolensis* Welw.

become paralyzed before death as the victims of the poison test fall to the ground shortly after drinking the mixture. As I have fully described in another publication the manner in which this extraordinary custom is carried on, I shall not repeat it here.

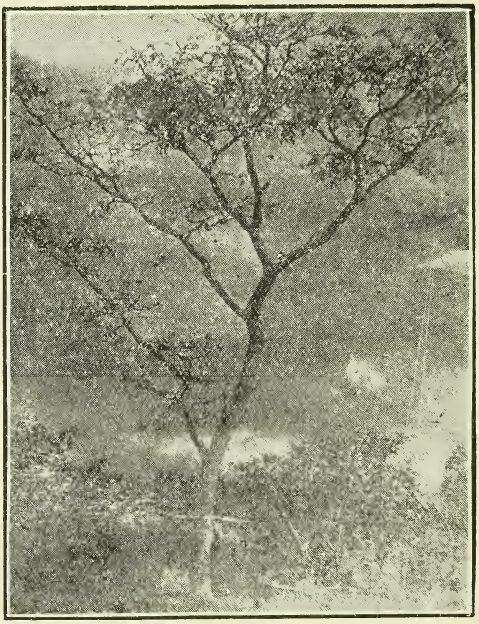

Fig. 8.—*Burkea africana*, Hook.

Ocati, *Cassia occidentalis*, L. Roots boiled in water and the decoction administered as an anthelmintic.

Ososo, *Entada abyosinica*, Stend. Leaves pounded up and applied raw to limbs swollen from any cause, but generally attributed to witchcraft. The ashes from the burnt leaves are applied to the umbilicus of newborn children.

Usonge, *Albizzia anthelmintica*, A. Brogn. Generally esteemed a specific for the diseases of domestic animals (dogs, etc.). The roots are also boiled to make a mouth wash for ulceration of the gums, sinuses from decayed teeth, etc. It is also used in some way I cannot learn for headache and neuralgia.

Okangato, *Acacia reficiens*, Wawra. Leaflets boiled with salt and given for dysentery.

ROSACEÆ.

Usia, *Paranarium mobola*, Oliv. The bark is employed in debility from any cause as a stimulant and tonic. The usual method is to boil the bark and inhale the steam.

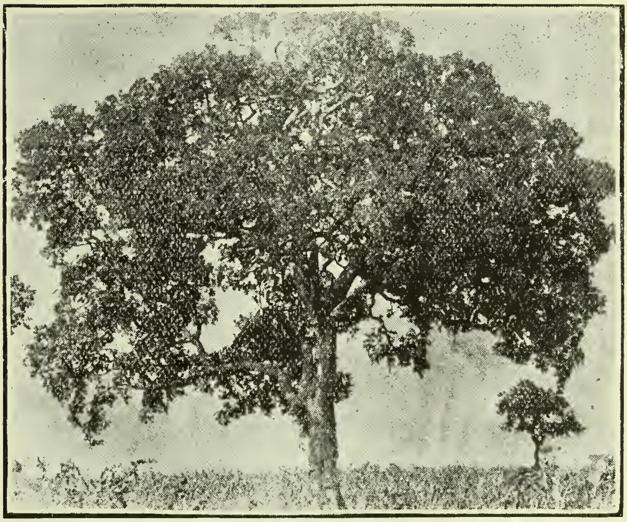

Fig. 9.—*Paranarium mobola*, Oliver.

MYRTACEÆ.

Ongayawa, *Psidium sp.* Infusion of leaves employed as an internal astringent in diarrhea. Green fruit eaten for same purpose.

Ulembaputu, *Eucalyptus sps.* Decoction of leaves drunk by natives for intermittent fever.

COMBRETACEÆ.

Ungolo, *Terminalia angolensis*, Welw. Inner bark of roots considered a remedy for diarrhea.

RUBIACEÆ.

Ocilavi, *Gardenia jovis-tonantis*, Hiern. Bark sometimes used as a bitter tonic. As its names implies, it is believed to be a charm against lightning.

VERBENACEÆ.

Usilusilu, *Vitex sp.* The leaves are boiled, pounded, and applied to the abdomen for colic. The plant is also used in some form to treat conjunctivitis.

LABIATÆ.

Ondembi, *Aeolanthus sp.* Applied as a stimulating poultice in anemia and cachexia.

Okatetembula, *Tinnea antiscorbuta*, Welw. This name was first given me for a mint (*T. antiscorbuta*), the leaves of which are boiled in water and used as a mouth wash, but in another part of the country the term "Okatetembula" is used to indicate *Uapaca benguellensis*, *q. v.*

COMPOSITÆ.

Ocisekua, *Tarchonanthus camphoratus*, L. Used in malarial fever. Bark ground up and drunk in decoction and odor inhaled.

Kayelelindi, *Calendula, sp.* Leaves boiled and applied as a poultice to strains, bruises, etc.

PLUMBAGINACEÆ.

Nakanganga, *Plumbago zeylaniea*, L. The roots are applied to the skin as a blister, and small quantities are also placed in the cavities of decayed teeth to destroy the nerve. In Bihé the name "Nakanganga" is applied to a small leguminous shrub which I have never seen described. It is very poisonous, and I know of one instance in which a man accidentally killed his child by the administration of a small quantity of the leaves (mistaken for another plant) steeped in water.

EBENACEÆ.

Owelele, *Maba mualala*, Welw. Infusion of leaves and twigs used as an anthelmintic.

APOCYNACEÆ.

Ocimbinga, *Strophanthus sp.* The milky juice (which was formerly used to poison arrow heads) is applied to sores. The fresh exudation from the roots is used.

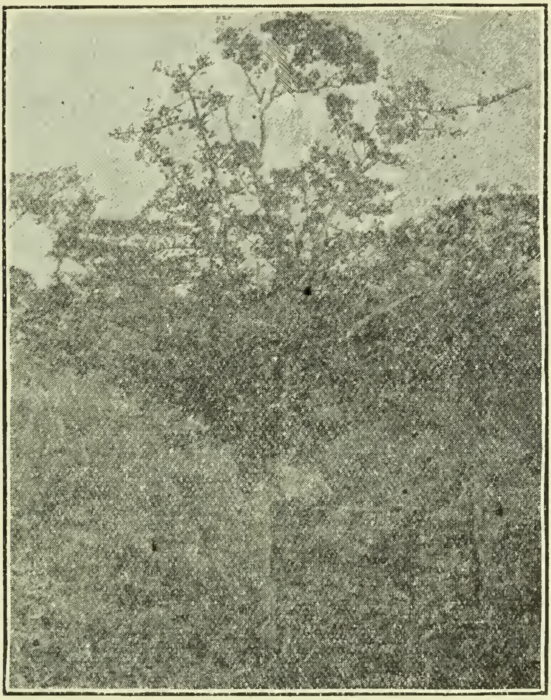

Fig. 10.—*Gardenia jovis-tonantis*, Hiern.

LOGANIACEÆ.

Upole, *Strychnos sp.* Roots boiled, mixed with maize or millet beer and drunk for pains in the bowels.

CONVOLVULACEÆ.

Olucatu, *Cuscuta sp.* Used for muscular pains. Boiled and drunk; also applied locally.

SOLANACEÆ.

Alulangue, *Atropa sp.* The fruit pounded up and mixed with salt is applied locally for the "goat itch," which kills goats unless treated. The fruit is also cut in two and applied to the body in case of severe pain in persons suffering from malaria.

Olundungu, *Capsicum sp.* Sometimes given to expel worms.

Ekaya, *Nicotiana tabacum*, L. Is almost universally used either smoked or in the form of snuff. It is never chewed. Medically it is put on cuts and fresh wounds and the roots used in the treatment of trachoma.

CHENOPODIACEÆ.

Etiambulu, *Chenopodium ambrosioides*, L. This is the great panacea of the partially civilized blacks and half castes. Boiled and drunk for headache, pains in the chest, stomach, etc., also for worms and various ailments. The bush natives are coming to use it more than formerly.

EUPHORBIACEÆ.

Omolo, *Ricinus communis*, Müll. The oil is used in the treatment of "ukau," a skin disease resembling eczema. The leaves are pounded up and inserted in the vagina to make a retained placenta come away.

Osoma, *Euphorbia rhipsaloides*, Welw. The milky juice mixed with water is taken as a demulcent and expectorant in chest diseases. The terminal joints of the branches are also eaten raw for the same purpose.

Ocimbolo, *Jatropha curcas*, L. Seeds chewed up and swallowed as a purgative.

Ombula, *Uapaca benguellensis*, Müll. Infusion of bark and leaves used for nosebleed, being snuffed into the nostrils and held in the mouth. Also as a mouth wash for ulceration of the gums. Diarrhea is likewise said to be cured by it, the infusion being drunk for this purpose.

CANNABINEÆ.

Epangue, *Cannabis sativa*, L. Hemp smoking is common. Medically the effects are held to be those of a tonic.

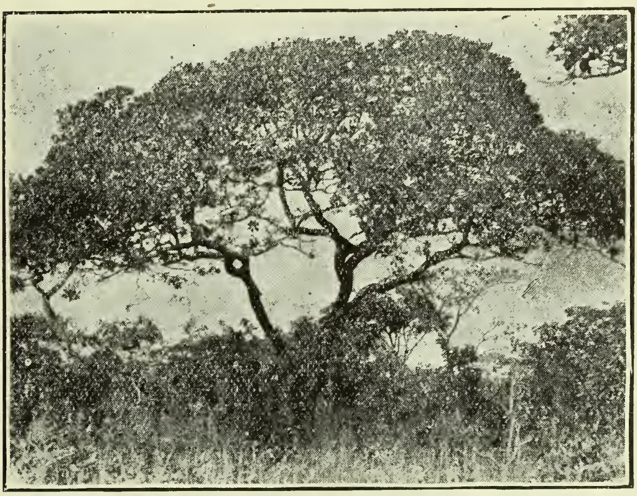

Fig. 11.—*Uapaca benguellensis*, Müll.

ARTOCARPEÆ.

Ulemba, *Ficus psilopoga*, Welw. The leaves and bark are made into poultices for pains of almost any description.

Ukuyu, *F. mucuso*, Welw. Different parts of this tree are used as ingredients in mixtures used to treat various complaints supposed to be due to witchcraft.

MONOCOTYLEDONS, GRAMINEÆ.

Owangu. This is a general name for grass. Species of *Eragrostis*, *Setaria*, and *Phyllorachis*, which are used in women's diseases, but more especially in fetish rites. A coarse grass (which I am unable to determine), called "Ohotahota," is burned and the smoke inhaled for headache. A grass of which I have not seen the flower or fruit, is used in stomach troubles. The root is the part employed. I have also had specimens near *Pannicum* and *Paspalum* brought to me, but with very vague information as to their medical uses. Grasses being difficult to recognize, the above list is by no means complete.

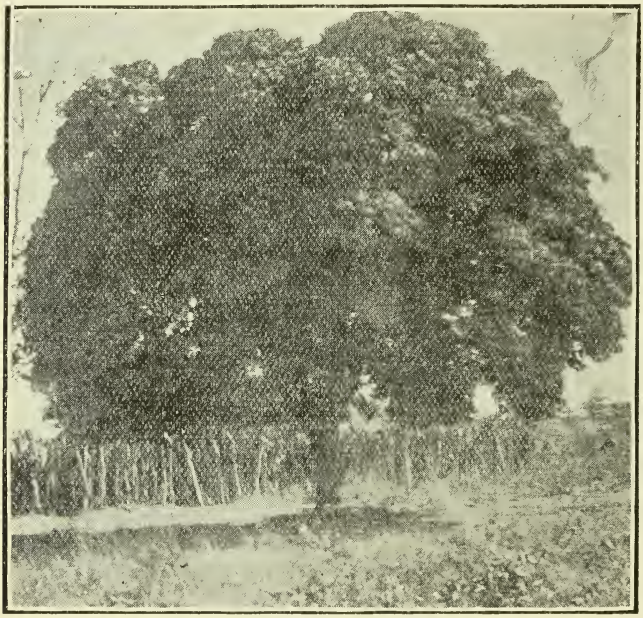

Fig. 12.—*Ficus psilopoga*, Welw.

CYPERACEÆ.

Osoka, *Cyperus sp.* Roots eaten raw as an anthelmintic.

Ocimbu, *Papyrus antiquorum*, L. Ashes mixed with other medicines to increase their efficiency. Several other sedges are used in witchcraft and fetish rites.

LILIACEÆ.

Ocandala, *Aloe sps.* The thick, fleshy leaves are chewed and swallowed to produce catharsis after overeating, and the juice is also employed in the treatment of sores.

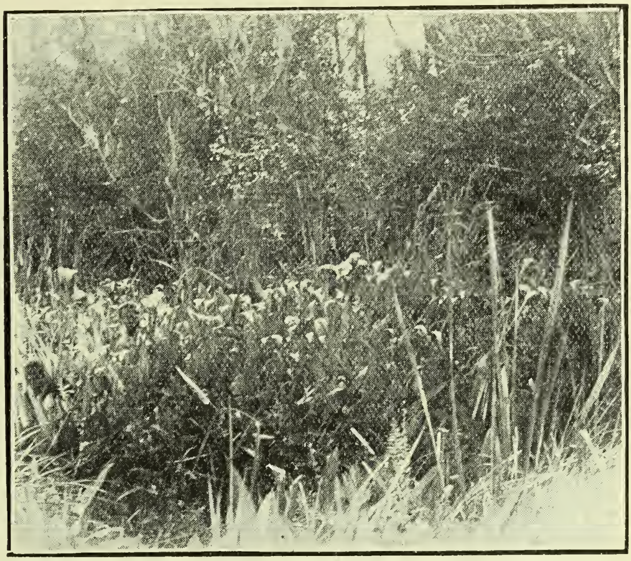

Fig. 13.—*Richardia africana* growing in swamp.

Onjelele, *Asparagus sp.* (*? racemosus*). Supposed to be a strengthening application to the body in cachexia.

Ombungululu, *A. africanus.* Infusion drunk to cure pains in the chest.

AROIDEÆ.

Evongevonge, *Richardia africana.* Leaves and flowers mashed up and applied to paralyzed limbs.

PALMACEÆ.

Ondende, *Elaeis guinensis.* The oil is applied to sores.

Ocisome, *Metroxylin sp.* Is used medically, but just how I cannot learn.

CORYPHINEÆ.

Okasalala, *Phœnix spinosa.* Ashes used in treating weakness of old age.

IRIDACEÆ.

Sipesipe, *Gladiolus sp.* Roots boiled, mixed with meal, and taken for cystitis or any other bladder trouble.

BROMELIACEÆ.

Ociteke, *Amomum sp.* Seeds eaten for abdominal pains.

Ovomomis, *Costus sp.* Used same as preceding.

SCITAMINEÆ.

Ucalo, *Canna sp.* Used same as two preceding.

CRYPTOGAMIA, POLYPODIACEÆ.

Ocinjamba, *Polypodium sp.* Boiled and steam used as vapor bath in hyperpyrexia.

OPHIOGLOSSACEÆ.

Ocinyene. Roots used like ergot to hasten childbirth or procure abortion.

Ocusitu, *Adiantum sp.* Used like foregoing.

A glance at the preceding review shows (1) the bush natives of west Africa use a large variety of plants as medicines; (2) as a rule they have a separate remedy for each disease; (3) their internal remedies are almost exclusively administered in the form of decoctions or infusions; (4) they have faith in many inert substances. The study of the plants used by a savage people like those here observed throws an interesting sidelight on the evolution of materia medica and therapeutics.

A study of this kind must necessarily always remain incomplete. Since writing most of the foregoing notes, a sedge, a mint, two fungi, an orchid, an alga, a species of *Spondias*, several *Umbelliferæ*, and three additional *Compositæ*, all purporting to possess medicinal virtues, have been brought to me. These, with other new material, I hope to discuss at some future time. Only a few of the diagnoses of the plants mentioned in the foregoing list have been confirmed by specialists, but I hope the errors found will be inconsiderable.

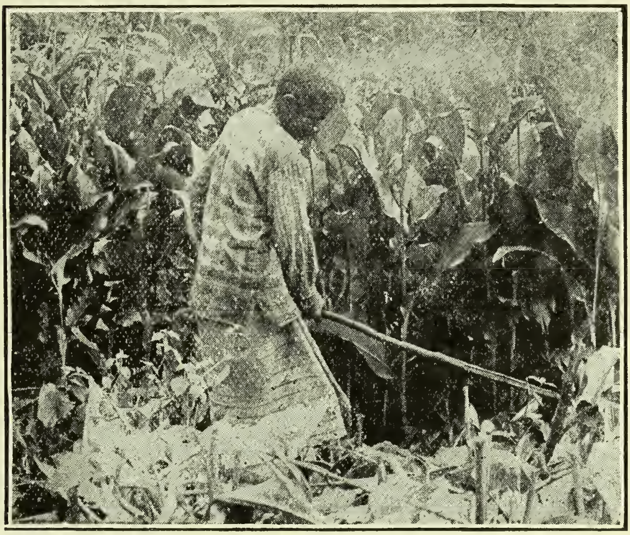

Fig. 14.—Cannas growing in jungle.

The illustrations are from photographs taken especially for this paper by Mr. W. E. Fay, B.A., with the exception of Figs. 3, 12, 13, and 14, which are from photographs kindly given to me by Mrs. E. D. Woodside.

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BERIBERI.[1]

BY P. A. LOVERING,

Medical Inspector, U. S. Navy.

It has been suggested to me that I write a short sketch of beriberi based upon my observations of the disease in the Orient and elsewhere. I have felt some hesitancy in acceding to this request, as I know that the members of a society for the study of tropical diseases are better acquainted with the recent literature of beriberi than I am. It is likely, however, that I have seen and treated more cases of beriberi than many of you, and perhaps some of my recollections may serve to occupy an hour.

I saw the first cases of beriberi many years ago on my first cruise to Japan, when they were shown me by Dr. Simmons, an American physician long resident in that country, who was one of the earliest writers in English upon this disease. He had been long employed by the Japanese government, and at the time of my visit was in charge of a hospital near Yokohama. I well remember his taking me through the wards where there were many patients suffering with beriberi, or kakke, as it is called in Japan. Some years later, on my second visit to the East, I saw the disease again, and on my recent tour of duty in Cavite I again renewed my early recollections. At different times I have seen the disease in naval hospitals in our own country, and have treated it on board ship.

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[1] Read by title at the annual meeting of the American Society of Tropical Medicine, held in Philadelphia, March 21, 1906.

In a short article I cannot dwell long upon the history of the disease or upon the theories which have been put forth to explain its occurrence, but it is impossible to omit entirely their consideration.

Beriberi is mainly a disease of warm countries, but well-marked outbreaks have been observed in temperate regions in almost every part of the world, as shown by epidemics in insane asylums in Ireland and in our own country, and the rather frequent occurrence of it upon fishing vessels upon the banks of Newfoundland. It is not improbable that many cases of the disease have been overlooked or wrongly diagnosed, and even in our own country we may rather unexpectedly meet with it. This is particularly liable to happen in our seaport towns among the sailors who have just landed after a long voyage from the tropics. In London it is not uncommon to see cases among the Asiatic sailors on the steamers from the East.

Within the last few years it has been universally recognized that beriberi is a multiple neuritis affecting the peripheral nerves both motor and sensory. In severe cases the vagus and its branches are also affected. More rarely other nerves, as the phrenic, are attacked. The symptoms are those of paralysis, both of motion and sensation, usually attended with edema, and when the vagus is implicated there are severe cardiac complications. While we know that beriberi is a multiple neuritis, there is great difference of opinion as to the cause. We do not know whether it is animal or vegetable, protozoön or bacillus, and in spite of an immense amount of work we know little more of its etiology than we did a generation ago.

Theories of all sorts have been proposed to account for the disease, and I will rapidly mention some of those most generally supported.

The malarial origin and later the hook-worm theory were stoutly maintained, but have long since been abandoned. Many observers believe that it is a disease of nutrition, but they do not agree as to what particular article of the diet is at fault. There are at least three of these theories which are still actively supported:

(*a*) Deficiency in the nitrogenous articles of the diet is believed by many to be the cause.

(*b*) Deficiency in the fatty articles of food is ascribed by others as the cause.

(*c*) A diet containing too much rice, rice of an inferior quality, or improperly prepared, is still believed by many to be the cause.

Certain epidemics or outbreaks have occurred which seem to support each of the above theories, but no one of them will satisfactorily explain any large number of outbreaks.

I believe that the theory of Scheube, Baelz, and others is the one most likely to be correct, and explains most satisfactorily the largest number of cases. They think that beriberi is an infectious disease due to a living germ of yet undetermined nature, that it can be carried from place to place, and where it meets a suitable field with favorable conditions of moisture, heat, and overcrowding, very probably aided by a meager diet, it will multiply, and entering the body either by the lungs or stomach produces a poison or virus which causes a neuritis. According to this theory a new locality may become infected and a new outbreak of the disease occur. The views of Dr. Hamilton Wright are probably familiar to you and are now looked upon most favorably by many. He believes that the specific organism is ingested with food or drink, multiplies in the stomach and duodenum, causing primarily a gastroduodenitis, and elaborating a virus which poisons the peripheral terminations of the vagus and other nerves.

We see, then, that there is a great diversity of opinion as to the etiology of beriberi, one school believing that it is a disease of nutrition, and the other that it is an infectious disease due to some germ not yet discovered. While the first theory is perhaps more generally believed, I think the second is more probably the true one. Scheube, one of the greatest authorities on tropical diseases, and who observed very many cases of the disease during his long stay in Japan, gives the following cogent arguments for regarding it as an infectious disease:

1. That strong, well-nourished young males are most frequently attacked, and are particularly liable to the severest forms of the disease.

2. Beriberi has narrowly defined districts in which it is most prevalent. How closely limited and circumscribed these areas may be is shown by the fact that the disease may be confined to certain wings and stories of the same building.

3. The conditions of the weather, heat and moisture, exert great influence upon the prevalence of the disease.

4. During recent years the disease has shown a great tendency to spread, and is now far more widely distributed than it was fifty years ago. This extension of the disease has taken place without any change in the food of the people. It is far more prevalent in Japan than it was a generation or two ago.

5. Like other infectious diseases beriberi shows a marked tendency to periodic fluctuations, quite independent of any changes in food. It appears in a country, prevails severely for a while, then diminishes in frequency and severity, only to break out again after an uncertain interval of time.

Beriberi is undoubtedly carried by man like other infectious diseases. Coolies, convicts, and laborers have carried it to places where it was previously unknown, and have served as foci from which it has spread, infecting the district.

In the tropics the dark-skinned people are more often attacked than white residents, and in the East you will see few cases among Europeans and Americans. This immunity is due less to race than to more favorable conditions of life, and when white men are exposed to exactly the same conditions they suffer as much as the dark-skinned people. In the outbreak at Tuscaloosa, Alabama, the percentage of the white patients who were attacked was greater than that of the black.

We know that there are certain conditions which favor the development of beriberi, and the most prominent of these factors are moisture, heat, overcrowding, and, in general, poor hygienic surroundings. In the tropics the rainy season will witness more cases than the dry, and when the disease becomes endemic it is far more frequent in low-lying localities, and particularly where the soil has been recently disturbed. Crowded, poorly ventilated habitations afford very favorable soil for the development of beriberi. Frequent outbreaks have occurred in barracks, asylums, and prisons. Similar conditions on board of ships have preceded the appearance of the disease. In Manson's well known work there is a graphic account of a vessel in London where beriberi attacked the Indian crew, and where the crowded forecastle with its heated, steaming atmosphere produced just the conditions favorable for its development. The crews on the fishing vesels which go to the Banks of Newfoundland are frequently attacked, and there are many outbreaks recorded both by American and French writers.

Turning now from the etiology of the disease to a consideration of the clinical features, we find that there is much variety in the symptoms which mark the invasion of beriberi. Catarrhal symptoms of the air-passages, stomach, and intestines are rather frequent, and with them is languor and heaviness in the legs, with some loss of power. The arms may be similarly affected, but usually to a less degree. Anesthesia of the skin with tenderness of the underlying muscles has been reported by some observers. The heart may be involved, and palpitation is frequent, often accompanied with shortness of breath. These symptoms I have described are quite characteristic and typical but they are by no means constantly present, and often are so mild that they pass unnoticed. This is particularly common when the patients are Asiatics, who persist in working until the disease is well advanced, and who usually cannot give a very good account of the attack owing to their ignorance of the physician's language. Dr. Hamilton Wright believes that symptoms of gastroduodenitis quite commonly exist, particularly in the acute type. Very recently I had the opportunity of talking with Baron Takaki, who is well known for his successful efforts in stamping out the disease, which was frightfully prevalent in the Japanese navy twenty-five years ago. I asked him if gastrointestinal symptoms were common at the beginning of the disease, and he told me that they were, ascribing them to the diet, which contained so much rice. I think then that we may assume that gastroduodenitis is a common initial symptom, especially in the acute form of the disease.

You will find several different varieties of beriberi given by different writers, but for our purpose I think it is more convenient, if not so scientific, to divide it into the three types of acute, subacute, and chronic. The acute type is a natural and well-defined variety. The subacute type includes a great variety of cases, some almost as severe as those of the first variety, and others which are mild from the start. The chronic forms are also manifold, but all have the common feature of persisting for a time varying from months to years.

The acute form is mostly seen in the tropics, and even there it is not very common, being much less frequent than the other varieties. Symptoms of gastroduodenitis are particularly frequent in this variety. It is shown by a feeling of heaviness and weight in the stomach, some tenderness on pressure, and perhaps nausea and vomiting. Even this early in the disease, or at the longest in the course of a day or two, there is some disturbance of nerve function. The knee-jerks disappear, hyperesthesia, paresthesia, or anesthesia is noticed, most marked in the front of the legs. The forearms are also affected, but less frequently. Along with the disturbances of sensation may occur paralysis of the motor nerves. These, too, are more common in the legs, less frequent in the upper extremities. Some anasarca is often present, but frequently nothing more than edema of the front of the legs. These symptoms are commonly present in greater or less degree, and are more marked if the case survives several days.

The most important and characteristic symptoms of this type are those manifested by the heart. Palpitation and then labored action of the heart is pronounced. The area of impulse is much increased to the right and in the epigastrium, the vessels of the neck throb violently. On auscultation the rhythm is found much altered and murmurs are present.

Shortness of breath, soon increasing to marked oppression, and extreme dyspenea are almost invariably present. The patient complains that the chest feels as if compressed by an unyielding band, or in other cases as if the chest would burst asunder.

The heart soon becomes dilated, the lungs engorged, and the cardiac oppression and dyspnea increase to a veritable agony, perhaps accompanied with persistent thirst and vomiting. The pulse is rapid, intermittent, and feeble, even when the action of the heart seems so violent. Cyanosis appears, the skin grows cold, and death soon ends the patient's tortures.

In addition to these symptoms the diaphragm, larynx, and pharynx are in some cases paralyzed. The patient always dies; sometimes he may linger a week, rarely so long, generally dying in four or five days, and in the severest form in a few hours. The severity of the symptoms in this variety is due to the rapid and fatal poisoning of the vagus nerve, both cardiac and pulmonary branches being affected. beyond repair. The involvement of the vasomotor nerves, with the effusions into the serous cavities of the chest, adds much to the patient's sufferings.

The subacute form is much more common than the acute variety, and with the chronic includes the cases you generally see in the hospitals in the East.

The subacute variety embraces cases with very different clinical features. Some are almost as severe as the acute type, but are not so rapidly fatal, others recover entirely, while very many, either directly or after a period of greater or less improvement, pass into the chronic form. The invasion of this variety is usually gradual, and the symptoms slowly develop.

Usually in the front of the legs there is some perversion of sensation—pricking, smarting, burning, itching, and formication are all common. In some cases there is hyperesthesia, but this is not so common as paresthesia. Anesthesia more or less marked is almost always present, and is superficial rather than deep. These disturbances of sensation are most marked in certain well-defined regions of the body. The skin in front of the legs over the tibiæ, on the dorsum of the foot, the front of the thighs, the fingers and forearms, and around the mouth are the favorite sites.

Muscular palsies also develop; at first there may be nothing more than lassitude or a feeling of heaviness, but this soon increases to loss of power. The extensor muscles of the thigh, leg, foot, and forearm are particularly liable to be paralyzed. Some of the facial muscles are, also, often affected. While the flexor muscles do not escape they are affected to a much less degree. In consequence of these paralyses of the extensors there is foot-drop and wrist-drop. The toes point to the ground and the wrist and fingers are bent. You will see some cases, too, in which the mouth is open from paralysis of the masseter and temporal muscles.

The paralysis varies in degree; in some cases it is only slight, and the patient can walk and help himself, but in others it is so extreme that he is completely helpless and actually cannot move hand or foot. In my experience the trunk muscles are not so often involved. In some cases I have seen contraction of the gastrocnemii which were hard and tender. This contraction may occur in other muscles, and the tenderness on deep pressure is quite characteristic. The affected muscles atrophy and waste to a marked degree, and in what is often called the atrophic or dry form the patient is extremely emaciated. The legs are particularly apt to be atrophied, and the atrophy increases from above downward. The knee-jerk and the tendo Achillis reflex are often absent, as well as the other deep reflexes, while the superficial reflexes are retained. The affected muscles do not react to electrical stimulation either galvanic or faradic.

The sphincters of the bowels and bladder as a rule work normally.

There is another symptom which is present in most cases—edema, and often anasarca. The presence or absence of edema is the reason for the frequent division of beriberi into the wet and dry types, but I believe that there are very few cases in which some degree of edema does not exist at one stage or another. This edema is most common in the legs, on the inner side of the tibiæ, and on the dorsum of the foot, but may be found in any part of the body, and may be associated with collections of fluid in the serous cavities. Dropsy of the pericardium is most frequent, then hydrothorax and ascites. In well-marked dropsical cases the anasarca is pronounced and as prominent as in cases of acute nephritis.

While in subacute beriberi the heart is not so liable to be affected as in acute beriberi, some involvement of this organ is almost always found. Often there is nothing more than an irregular hurried action, particularly noticeable on slight exertion. So long as the patient keeps quiet he may have little discomfort, but if he walks rapidly the pulse jumps from 75 to 100 or more, becomes weak and irregular, and there may be some shortness of breath. In the severer cases the area of pulsation may be increased and there is throbbing of the vessels of the neck. The area of the heart's dulness is often increased, especially to the right, and on auscultation changes in the rhythm and murmurs are frequently heard. The course of the subacute cases is apt to be rather prolonged even when there is complete recovery, due to complete regeneration of the affected nerve tissue. It is usually several months before the patient is well. The anesthesia and other disturbances of sensation gradually pass away, the palsies of the muscles improve until nothing remains but a slight weakness, which in time also disappears. Loss of sensation and motion continues longest in the muscles of the leg, and may persist in a slight degree when the patient is well in other respects. The knee-jerk is lost for a long time, perhaps permanently.

The mortality in this type is low, and the patient usually recovers, or else the trouble assumes a chronic form. There are, however, certain cases of this type which are nearly as rapid in their course as cases of the acute type, differing from them only in being more prolonged. This type takes two or three weeks to run its course instead of a few days; death is due to the same cause, poisoning of the vagus; and the clinical features are very similar, but not quite so acute or rapid.

Relapses or recurrences are by no means rare in subacute beriberi. In Japan, after apparently complete recovery, the patient at the end of a year from the original attack is very liable to have a recurrent atttack, and these returns of the disease may occur for years. Exposure to unfavorable hygienic conditions, overwork, and poor food are all favoring factors for a relapse. Recurrent attacks as a rule are mild, but I have known death to occur in them.

A rather striking fatal case of relapse occurred in my own practice many years ago. I was on the old sloop of war *Brooklyn,* which was returning to New York from Japan. The machinery having broken down we were compelled to make the passage under sail. We left Nagasaki about the middle of September, and breaking our voyage at Honolulu for about two weeks, resumed our course for New York, going around Cape Horn. Our progress was slow, and it took us 141 days to reach the next port, St. Thomas. About ten days before we arrived there, when we had been at sea over four months, beriberi appeared on the ship. The only persons affected were the Japanese mess attendants, none of the white or black members of the ship's company being attacked. The Japanese were exposed to exactly the same environment as every one else, and had the same food as the officers. There was no possibility of their obtaining anything else to eat, and their diet was the same as mine, containing little rice and sufficient nitrogen. I do not believe that the ship was infected, and the only explanation of the outbreak was a recurrence of a dormant malady. One of the cases proved fatal, and the symptoms were as severe as in acute cases.

There remains for our consideration the third type, or chronic beriberi, which is a sequel of the subacute variety. A subacute case, when it does not recover entirely, may continue without any notable change and gradually pass into the chronic form, or there may be considerable improvement of all the symptoms, stopping short of complete recovery.

In still another set of cases the patient may have improved so much that he resumed work and kept at it for a while, then broke down, returned to the hospital, and, perhaps, after a while was well enough to work again. These relapses and partial recoveries may continue for years.

Whatever be the history of the chronic type, whether directly following a subacute attack or being a relapse after an interval of improvement or apparent recovery, there is considerable similarity in the symptoms and course of the disease. In those subacute cases which assume the chronic form the anesthesia, paralyses, and loss of reflexes all persist. Edema is usually present, and in some cases there is anasarca. The heart is usually enlarged, and there is palpitation, with rapid, irregular, and feeble pulse. The cardiac symptoms increase in severity, the edema becomes more pronounced, and the paralyses more marked. The patient dies in a sudden collapse, or is carried away by some intercurrent disease.

When the chronic form appears after an interval of more or less improvement, there is a return of the original symptoms which characterized the first attack, and which I have already described to you at considerable length. Chronic beriberi is the type you usually see in visiting the hospitals in Japan and other Asiatic countries. I have seen wards full of these patients, and was impressed by the great variety in the clinical features they presented. It is hard to realize that they were all suffering with the same disease.

These cases of chronic beriberi can be divided into the atrophic or paralytic form and the dropsical form, or, as they are often called, the dry and wet forms. There are also many cases of a mixed type which present both paralytic and dropsical symptoms, sometimes the one set, sometimes the other predominating.

The typical paralytic cases present a very characteristic appearance. The legs are much wasted and the shin bones stand out prominently. The muscles of the arm are less wasted, but I have seen some cases in which all the voluntary muscles were more or less affected. Along with this atrophy there is loss of sensation and power. The loss of power from paralysis of the nerves and atrophy of the muscles may be so great as to simulate paraplegia, and you will see the patient dragging himself painfully along with the aid of a staff, the legs spread well apart, toes pointed down, and the feet striking the ground with a flap. Wrist-drop is as pronounced as in lead palsy. With all this paralysis the man does not seem very sick, he eats pretty well, and has control of his bowels and bladder.

The heart is very apt to be affected, and on the slightest exertion you will find palpitation, increased area of pulsation, and a quickened pulse. Combined with these symptoms is increased area of dulness, murmurs, and changed rhythm.

The other type is equally striking in appearance. The dropsical cases are as swollen as the atrophied are shriveled. There is general edema; face, body, legs, and arms are all puffy and distended. There may also be ascites and effusion into the chest and pericardium. When the dropsy is so extensive there is very commonly cyanosis and dyspnea. The patient is generally confined to his bed, but you will find on examination that there is paralysis and ataxia present. While the digestion may not be much impaired, the urine will be scanty. Examination of the chest will show an involvement of the heart quite similar to that in the atrophic form.

In still another set of patients will be found a mixed set of symptoms, including the atrophic and paralytic symptoms, accompanied with some edema. In my experience this is perhaps the most frequent class of cases seen.

Provided the nerves are not too seriously affected there may be complete recovery, such as you find in postdiphtheric neuritis, but very often death may suddenly occur from collapse due to cardiac paralysis. It happens, too, not infrequently, that the patient may recover a fair state of health, but be left with an enlarged heart or atrophied limbs.

Pathology.—The clinical symptoms of beriberi are due to the direct action of the poison upon the peripheral termini of the nerves. Certain nerves are peculiarly liable to be attacked —the musculocutaneous of the legs, the branches of the sciatic, which supply the legs and thighs. Later the nerves of the upper extremity and of the face are affected. It is more unusual to find any involvement of the nerves supplying the muscles of the trunk, the intercostal and diaphragm. The larynx is quite often affected, and occasionally hearing and sight are lost. The poisoning of the nerves causes the paralysis of sensation and motion which always exists, provided the patient lives more than a few hours.

The virus of beriberi very often attacks the nerves of the heart, both the branches from the vagus and sympathetic system. The edema is probably to be explained by the paralysis of the nervi vasorum, and it is interesting to note that the edema occurs first in front of the legs, over the muscles which are earliest affected with paralysis.

Fatty degeneration of the myocardium and the voluntary muscles, due to the action of the virus, and subsequent neuritis are constant appearances in chronic cases.

Dr. Hamilton Wright describes a gastroduodenitis occurring in acute cases attended with congestion of the mucous surface and the presence of the bacilli.

There is often congestion of the liver, kidneys, and spleen, but no very characteristic pathological changes are generally present aside from the degenerations of the nerves and muscles.

Prognosis.—The prognosis of beriberi varies greatly according to the type and locality. Acute cases always die. Subacute cases rarely die, but there may be considerable mortality in chronic cases, both from the disease and from intercurrent affections.

The prognosis depends mainly upon the extent to which the heart is involved. So long as this organ is not much damaged the prognosis is good, even when the paralysis and other symptoms are severe. Another symptom quite as unfavorable as those coming from the heart is paralysis of the diaphragm due to implication of the phrenic nerve.

While in Japan the mortality does not exceed 4 to 5 per cent, in Brazil it has been as high as 50 to 60 per cent. In the outbreak in the Tuscaloosa Insane Asylum the mortality was about 30 per cent.

The diagnosis of beriberi in a country where the disease is prevalent does not present much difficulty in the subacute and chronic cases, but in the acute cases death has often occurred unexpectedly when the cause was not suspected, as the paralysis and edema may not be at all marked.

Among whites in the tropics many cases of alcoholic neuritis are called beriberi, and there may be some difficulty in diagnosing between the two affections, but in alcoholic neuritis the edema and heart complications are absent.

I have seen a case of acute nephritis with cardiac complications wrongly diagnosed as beriberi, but the examination of the urine soon corrected the error.

Treatment.—As Scheube says, there is no specific cure for beriberi, but much can be done for the patient.

All recognize the importance of removing the sick man from the place where he contracted the disease, and if possible from the locality or district. If cases occur on a ship they should be sent on shore, and those developing on land should be removed to a high, well-ventilated situation, and as soon as possible be sent to a cooler climate.

Salines are probably more generally given than any other class of drugs, especially at the onset of the disease, sulphate of magnesia or soda being given in sufficient doses to move the bowels thoroughly. They do relieve the constipation and reduce the edema.

For those cases in which the heart is affected, and they include the large majority of all you meet, digitalis, I believe, is the best drug to be used. It steadies and strengthens the heart and also relieves the edema better than any other agent. You can combine it with a diuretic, as acetate of potash, and the results are often very satisfactory.

In the acute cases in which there is great cardiac insufficiency, as shown by the rapid, feeble pulse, violent palpitation, dyspnea, and cyanosis, I have taken 10 to 12 ounces of blood from the arm, and repeated it after some hours. It gives great relief to all the symptoms even if they recur later. This form of treatment has been much used in Japan, and is highly recommended. In chronic cases electricity is a useful application to the paralyzed muscles, and both the faradic and galvanic currents are used. It should be employed only in the later stages when the acute symptoms have subsided.

Strychnine, arsenic, iron, and other tonics are useful, but probably exert only a general effect in improving the strength of the patient. The usual attention should be paid to the diet, which should consist of easily digested nutritious food containing a liberal amount of nitrogen. Rice is a poor food for a beriberi patient, while beans are much thought of in Japan.

Prophylaxis.—I will close this rather lengthy article with a few words as to the prophylactic measures to be adopted when the disease appears on a ship or in an asylum, or when a district seems to be infected.

When cases have appeared on a ship, as careful disinfection should be practiced as in the case of other infectious diseases. Especial care must be given to the disinfection of the sleeping quarters by the use of formaldehyde, sulphur, and other agents. All bedding, clothing, and bunks should be as carefully sterilized as in an outbreak of plague. The sick should be removed from the ship, if possible, and if this is impracticable they should be isolated on deck and their stools disinfected, as there is a possibility of their containing the pathogenic germs.

If an outbreak occurs in a prison or an asylum, we should consider the apartments infected which the sick have occupied. There should be the most thorough disinfection of these rooms by cleansing, scraping, and the use of suitable disinfectants.

I recently learned of an outbreak at Bilibid prison in Manila, which has between 2000 and 3000 inmates, who are housed in many separate buildings. One building became infected, and many of the occupants were attacked. All the ordinary methods of sanitation and change in diet were of no avail, until the building and all its contents were most thoroughly disinfected, when the outbreak ceased. Similar cases have been recorded so often as to leave no doubt that a building or even a single story may become infected. When a district or locality becomes infected the problem is more difficult. The houses should be built on high ground, if possible, with ample openings for light and air. The lower floor should be cemented so as to prevent dampness and favor thorough cleaning. The drinking-water and that used in the kitchen should be boiled and care taken to prevent the infection of food, cooking utensils, and table ware. It is highly probable that infection may be carried through the feces, and careful attention should be given to them so that the disease may not be spread. We should use very similar measures to those we employ with cholera and typhoid stools.

Glossina palpalis wellmani: a new Tse-Tse Fly which disseminates human trypanosomiasis.

By F. C. Wellman.

Published under the imprimatur of the Amer. Soc. Tropical Medicine.

(Plate XII)

INTRODUCTION.

When in London last year I was asked by the Dipterologist of the British Museum, Mr. E. E. Austen, to see if I could establish the presence of Tse-tse flies in southern Angola, from whence no specimens had up to that time been received. On arriving at Benguella I accordingly made a short journey up the Katumbela River for this purpose, and succeeded in taking a number of specimens of a fly, some of which I sent to Mr. Austen for determination. I then supposed from my *amateur* examination of the flies that they were *Gl. palpalis* Rob.-Des., as I knew that this fly is the principal Tse-tse fly of the west coast,* although I had received some specimens of what I believed to be *Gl. morsitans* from the interior to the east.† I have since received a letter from Mr. Austen, however, concerning them, in which he writes as follows: "The present specimens show that the form of *Glossina palpalis* found in Benguella represents a new subspecies, distinct from the typical form. I have therefore named it in your honor—*Glossina palpalis wellmani.*" Although Mr. Austen's systematic description of the fly‡ is available, yet in view of the probable future importance of the animal to medical men practicing in southwest Africa, I have thought it worth while to in these columns call further attention to this new subspecies.

Glossina palpalis wellmani Austen (1905), Ann. and Mag. Nat. Hist, ser. 7, vol. xv, April, 1905, p. 390.

♂, ♀.—Frontal stripe pale ochraceous; thoracic markings much reduced, so that *the thorax in a well-preserved specimen appears spotted,* the antero-lateral markings taking the form of spots or blotches; the

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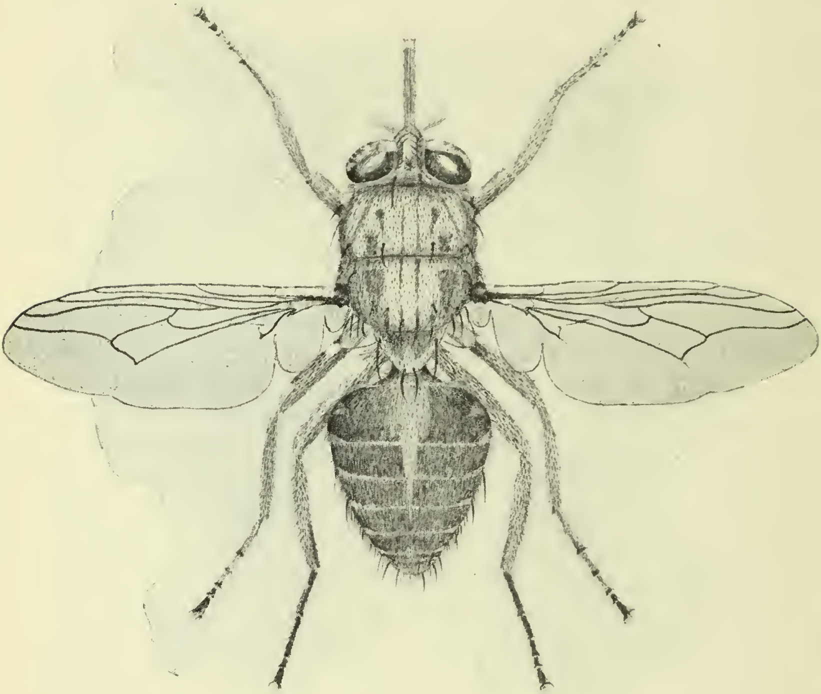
**Vide Austen,* A Monograph of the Tse-tse Flies, 1903, p. 75.

†*Vide* New York Medical Journal, August 12, 1905, p. 329. This collection was accidentally destroyed but I have sent to the same district for more.

‡Annals and Magazine of National History, Ser. 7, Vol. xv, April, 1905, p. 390.

spot immediately behind the inner extremity of the humeral callus on each side small, ovoid, or nearly circular, and especially conspicuous when the insect is viewed from above and slightly from behind; femora pale, the dark blotches much reduced.



Glossina wellmani.

Katumbela River, Angola, W. Africa; November, 1904 (*Dr. F. C. Wellman*). Six specimens (1 ♂, 5 ♀). Types in British Museum.

Remarks. In the paper containing his description just quoted Mr. Austen says, "The British Museum possess two females of *Gl. palpalis* from the Gambia (*Dr. J. E. Dutton*) belonging to a form somewhat similar to *wellmani;* in the Gambian form, however, the ground-color of the abdomen is paler and the thorax is less conspicuously spotted."

HABITAT.

My specimens were taken in a small district lying along both banks of the lower stretches of the Katumbela River, which empties into the sea near the port of Benguella, Portuguese West Africa. Mr. Austen writes,* "The above specimens are of especial interest as being the first recorded examples of any form of *Gl. palpalis* from Portuguese West Africa, and as showing that the range of the species in question, which has recently been stated by Laveran† to occur at Sengaleam (about thirty miles from Cape Verde), extends at least as far south as 12° 30′ S. lat. In all probability *Glossina palpalis wellmani* will eventually be proved to exist right down to the Cunene River, the southern border of Angola, if not further." Mr. Austen also wrote me suggesting that I try to establish the southern limit of the new fly. I have accordingly kept a sharp lookout for it and have made further inquiries concerning it with the meager result that I have received a single badly-damaged specimen of a Tse-tse fly purporting to come from the lower Kukema River, a couple of hundred miles to the east of the place where I found the subspecies under discussion, and a native report to the effect that a "fly belt" is known to exist on the upper Coanza still further inland. In view of Mr. Austen's belief that *Gl. palpalis wellmani* extends to the Cunene River I have visited the upper Cunene but failed to find any Tse-tse flies, and now, in accordance with his suggestion, written me when the flies were first discovered, I hope to, before long, visit the lower river with this object in view.‡ At least one species of Tse-tse is common in northern Angola and along the lower Coanza. This may very possibly be *wellmani*. The distribution of the species *palpalis* (with its subspecies and varieties) is now known to extend practically from Cape Verde to Damara Land.§

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*Ann. and Mag. Nat. Hist. *loc. cit.*

†*Comptes Rendus des séances de l'Academie des Sciences,* t. cxxxix, p. 659.

‡ Mr. Ralstone, of the Benguella Railroad, has recently informed me that a Tse-tse fly is found lower down on the Cunene River. This is very probably *Gl. palpalis wellmani.*

§ Austen, Reports of the Sleeping Sickness Commission of the Royal Society, No. vi, August, 1905, pp. 279-80.

NOTE ON BIONOMICS.

I can offer no extensive contribution to our knowledge of the habits of the subspecies. I present here a few special notes made at the time of collecting. "Although the district in which the flies were taken contains some game, including eland (*Orcas canna livingstonei*), kudu (*Strepsiceros kudu*), roan antelope (*Hippotragus equinus*), the duyker (*Cephalolophus grimmi*) and Speke's tragelaph (*Limnotragus spekei*), yet I believe that human blood forms the greater part of their food. This is undoubtedly true over at least a part of the 'belt.' Along the right bank of the lower Katumbela from a place called Esupua to a point half a day's march up the river there lies the great Benguella caravan route near which there is little or no big game and over which constantly pass great caravans of half-naked Bantu rubber, slave and ivory traders. At Esupua one may see half a dozen of these large caravans camping in one place. It is here that the flies are most plentiful. They hide in the tall grass and sedges near the river, also on stones, trunks of trees and vines, and among the leaves of the low trees on the bank. When a native is sent to the river for water the flies rise from their resting places as he passes and follow him seeking for an opportunity to bite. On several different occasions I followed natives going to the river to fetch water. One of these was bitten twice, three were bitten once each, and seven were not bitten at all. The Bantus say the bite is painful, and I noticed that if a fly settled on a porter's back the man always slapped himself as it began to insert its probosces. Some of the specimens I took had abdomens greatly distended with blood. The flies do not always remain so close to the river. The first one I saw was between three and four hundred yards from the river in thin 'desert' bush, consisting of *Acacia reficiens* and other thorny shrubs which afford practically no shade. I do not believe *Gl. palpalis wellmani* shares the dislike for human ordure which has been ascribed to its congeners. I have frequently seen it in and around the filthiest native camps at some distance from the river where it had evidently gone for the purpose of sucking human blood. I have made no observations on the life history. I dissected an incomplete larva out of the abdomen of a female. It was, I judge, rather more than 2.0 mm. long and of a light dirty yellow color. I have sent to Esupua to procure if possible some living flies and also some in alcohol so as to be able to send Mr. Austen a series of larvæ. The pupa I have not seen."

THE NEW FLY AND TRYPANOSOMIASIS.

I have lately seen three cases of human trypanosomiasis, all of whom had been frequently in the "fly belt" at Esupua. About 500 blood examinations were made, so that about three out of every 500 natives living in the districts adjacent to the Esupua "fly belt" harbor trypanosomes in their blood. The trypanosome found seems to be morphologically identical with *Tr. gambiense* Dutton. The shape of the posterior end, the arrangement of the controsome, nucleus and flagellum, as well as the "set" of the organism on the slide, correspond with the same points in *Tr. gambiense.* The protoplasm stains somewhat irregularly with Romanowsky, taking on a basophilic reaction. The centrosome stains a dark purple, and the flagellum, which stains pink, seems to rise from or near it. The nucleus lies near the middle of the body and often occupies more than two-thirds the width of the parasite. It is oval in shape and stains red like other chromatin material. Following are measurements of a stained specimen of the parasite:

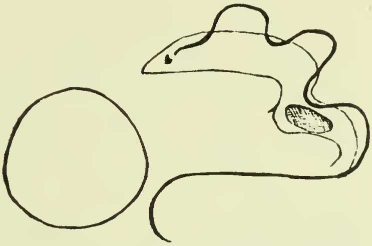

Fig. 1.—*Tr. ? gambiense* Dutton.

Length	(about)	24
Greatest width		3.5
Distance of centrosome from posterior end		3
Length of free flagellum	(about)	9
Largest diameter of nucleus		4

I have described and figured this parasite in another communication to which I refer the reader.* While sleeping sickness does not seem to be endemic as yet in the districts adjacent to the Esupua "fly belt,"† yet it is endemic in many situations in Angola from the north bank of the Coanza River clear to the Congo. As the country is being opened up it is inevitable that cases will from time to time be brought from the northern sleeping sickness centers to districts in the south, since many firms have trading posts and the Government has forts in both districts between which native soldiers and laborers are constantly being transferred. More forts are constantly being planted and trading posts established. The Umbundo-speaking Bantus, who number about 200,000, live to the east of the belt infested by the fly, and most of the males of these tribes are porters and rubber traders and constantly pass through the Esupua "fly belt," through which such occasional cases of trypanosomiasis ‡ from Malange, Cazengo, Ambaca, Dondo and other points in the sleeping sickness districts north of the Coanza, to which I have above referred, are carried by the activities just mentioned. Thus, the flies have and will have more and more favorable opportunities to become infected and to infect the Umbundos among whom I have recently demonstrated the occasional presence of trypanosomiasis. I believe for several reasons that this presence of trypanosomiasis among the natives of south Angola is a recent development. Some of these reasons are:

(1) Two years ago I examined a series of nearly 400 of these natives with a negative result.†

(2) Recently about 500 examined by me revealed three infected individuals in practically the same district.

(3) No cases of sleeping sickness *originating* in the district have yet been seen.

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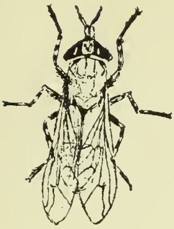
*Interim Report on Trypanosomiasis in Portuguese Southwest Africa.

†*Vide* Wellman, Notes from Angola (Note X, *Jour. Trop. Med.*, November 15, 1905, p. 327..

‡As sleeping sickness cases are occasionally transported, those in the earlier stages of trypanosomiasis are undoubtedly also brought south.

†*Vide Jour. Trop. Med.*, February 15, 1904, p. 53.



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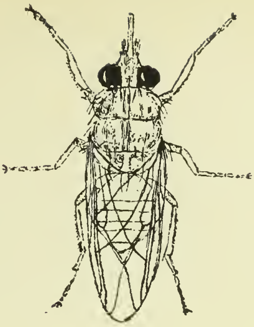

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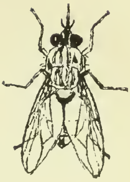

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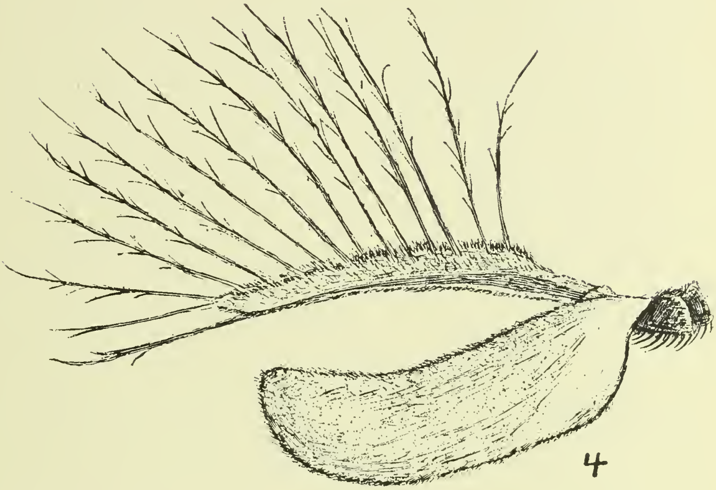

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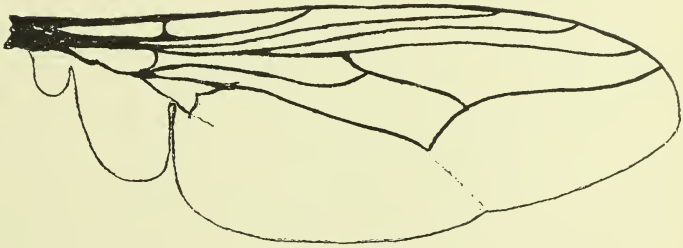

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FIG. 1. HÆMATOPOTA. FIG. 2. GLOSSINA. FIG. 3. STOMOXYS.

FIG. 4. RIGHT ANTENNA GL. WELLMANI. FIG. 5. WING OF GL. WELLMANI.

FIRST THREE FIGURES SHOW RESTING POSITION OF SOME BLOOD-SUCKING FLIES.

(4) Sleeping sickness is reported to be spreading *southward* through Angola.

In view of the considerations brought forward under this head, we need not be surprised (if we remember the history of the spread of scourges of Uganda and the Congo) if *Gl. palpalis wellmani* play in the near future a leading *rôle* in West African Medical History.

RELATION OF GL. PALPALIS WELLMANI TO OTHER TSE-TSE FLIES.

The Tse-flies are known from other members of the same family by the palpi forming a complete sheath for the proboscis, by the peculiar antennæ with branched hairs on the upper surface only of the arista, by the characteristic wing venation, by the wings closing over one another like scissors, by the grooved wing membrane and by the peculiar hypopygium of the ♂. Following are brief notes on the known species with some special remarks on the particular species to which belongs the fly we have been discussing.

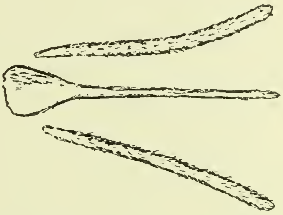

Fig. 2.—Proboscis and palpi of *Gl. palpalis wellmani* separated and magnified.

Genus **GLOSSINA** Wiedemann.

(1) *Glossina tachinoides* Westwood.—Described in 1850. Carries *Trypanosoma brucei* of nagana, the Tse-tse fly disease of game and domestic animals in Africa. Hind tarsi dark; abdomen buff with dark transverse bands, oblong pale area in center of second segment. Small species. Length 8 mm.

(2) *Gl. palpalis,* Robineau-Desvoidy.—Described in 1830. Carries *Tr. gambiense,* the parasite of human trypanosomiasis, which is considered to be the chief factor in sleeping sickness, and also *Tr. brucei.* Abdomen brown with triangular pale area in center of second segment. Darker than preceding and a larger species. Third joint of antennæ dark. Length 8-9 mm.

It is a variable species and under it falls the subspecies above considered:

Gl. palpalis wellmani Austen.—Described in 1905. Differs from type by having the frontal stripe pale ochraceous; thoracic markings much reduced, presenting a spotted appearance; spot behind humeral callus small, avoid or nearly circular; femora pale, the dark blotches much reduced.

There is also an unnamed variety which was at first designated *Gl. palpalis* var. *tachinoides* Westw., and was thought to represent a fly which, when true specimens were obtained, was recognized by Mr. Austen to be of specific rank (*Gl. tachinoides* Westw. [*vide supra*]), the variation from *Gl. palpalis* remaining unnamed at last accounts received here, and I therefore set it down for the purposes of this paper as

Gl. palpalis var. *a.*—It is distinguished from *Gl. palpalis* principally by its pale femora and a yellow median stripe on the abdomen.* There is also another variation from the typical *Gl. palpalis* which may be differentiated as follows:

Gl. palpalis var. *b.*—Femora still paler than foregoing; palpi pale except at tips; abdomen reddish brown with the pale area on second segment oblong.†

(3) *Gl. pallicera* Bigot.—Described in 1891. Color brown to mouse grey. Resembles *Gl. palpalis* except that third joint of antennæ is pale (orange buff). Length 8 mm.

(4) *Gl. pallidipes* Austen.—Described in 1903. Carries *Tr. brucei.* Mouse brown with longitudinal markings. Front and middle tarsi generally tipped with pale brown or yellow. Large species. Length about 11 mm.

(5) *Gl. longipalpis* Wiedemann.—Described in 1830. Differs from preceding in having black tips to last two joints of front and mid tarsi. Thorax olive grey; head broad; hypopygium in ♂ smaller, darker and more hairy than in foregoing species. Length 9-11 mm.

(6) *Gl. morsitans* Westwood.—Described in 1850. Carries *Tr. brucei.* Smaller and head narrower; hypopygium of ♂ also larger and paler than in foreging. Thorax pale in front with brownish longitudinal markings. Eyes in both ♂ and ♀ converge towards vertex. Tips of last two joints of tarsi dark, Resembles *Gl. pallidipes.* Length 7-9 mm.

**Brit. Med. Jour., loc. cit.*

†*Ibid.*

(7) *Gl. longipennis* Corti.—Described in 1895. Carries *Tr. brucei* and probably another trypanosome of camels and mules. Brownish; dorsum of thorax with four sharp, dark oval spots in form of parallelogram, two in front and two behind transverse suture. Bulb of proboscis brown at tip. Large species. Length 10-11 mm.

(8) *Gl. fusca* Walker.—Described in 1849. Thorax drab. No spots on dorsum of thorax as in preceding; bulb at base of proboscis not brown at tip (pale yellow); abdomen russet brown. Large pale species. Length 11-12 mm.

In conclusion, I wish to thank Mr. Austen, the well-known authority on Tse-tse flies, who kindly examined and described my collections and suggested to me the study of the distribution and pathological importance of the subspecies discussed in this paper.

THE AFRICAN POISON TEST AS OBSERVED IN THE PORTUGUESE COLONY OF ANGOLA, WEST AFRICA.

BY F. C. WELLMAN, M.D.

[Published under the imprimata of the American Society of Tropical Medicine.]

Introduction.—Much has been written by travelers from time to time regarding the very weird and extraordinary custom practiced by the savage tribes of tropical Africa for the purpose of settling disputes among themselves, and usually known as "the poison test." It has been remarked that these various accounts do not agree as to the details of the custom, and several writers have been accused of being inaccurate observers. The truth is that both the ingredients and manner of administering the test differ among different tribes, and the reason for the varying descriptions is to be sought in the facts themselves. It follows, then, that a description of the procedure holds good only for the people and district where it was drawn up, and it is therefore desirable that we should have careful studies of each variety of poison test in order that later a comprehensive survey may be made of a custom which has nearly depopulated whole districts and has been responsible for more deaths in Africa than have many important diseases. In the intervals of some patho-geographical investigations undertaken in Angola during 1904, the writer was able to collect some information regarding the locally employed ingredients and *modus operandi* of the ordeal as seen in the interior of that colony among the Umbundu-speaking Bantus. In accordance with what has been said above, the following observations must not be taken as necessarily true of the custom in other parts of Africa.

Name and Synonyms.—The name used by the Bantus is "Ombulungu." The Portuguese colonists generally refer to it as "Juramento." Synonyms are "a justicia de Deus," "Ombambu," "Wanga," "Mulianyi," "Bauve," "Muavi," etc.

History of the Custom in Angola.—The native history of the "Ombulungu" is of course nothing more than a mass of oral tradition, but after questioning a number of chiefs and old men I am inclined to the opinion that the custom did not independently originate among the Umbundus, but was introduced from the east or northeast.[1] I do not adopt this view from statements of the natives, although these bear out such an opinion, but after considerable study of the naive allusions to the custom contained in their proverbs, folk-lore, etc. The poison test has been known to the Portuguese from the time of their settlement of Angola, and stringent laws have been passed against it, it being contrary to the code for a captain-general or other administrative colonial officer to recognize the custom. This regulation is, however, unfortunately too loosely observed, and I know personally of one case where a lieutenant advised a native chief to go to the poison test with his accuser, and have been informed (in one instance by an army officer) of a number of perplexing cases sent to the "Ombulungu" by captains-general. One officer was even stated to have administered the ordeal himself, using two glasses of water, in one of which was dissolved tartar emetic. The custom has thus not only failed to disappear, but, according to those competent to judge, flourishes to-day in the interior almost as actively as in the past.

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[1] These remarks, of course, refer only to the rise of the custom in Angola. It is hardly necessary to refer to the well known fact that some form of trial by ordeal was a very widespread ancient custom not confined to Africa. Other ordeals—*e.g.*, by fire, boiling water, etc.—have long existed among the Zulus and other Bantu peoples.

Occasions of Appeal to the Poison Test.—An effort is generally made by the head men of a village to settle disputes amicably and satisfactorily to all parties. This can usually be effected except in three classes of cases:

1. Hereditary cases, or those which date back to a time preceding the memories of the disputants.

2. Mysterious cases of murder or other crimes of which there is no evidence to convict the accused.

3. Cases of alleged killing by witchcraft.

The first class of cases often date from the petty wars or plunderings of former chiefs. Under the second class fall many adultery cases, and the third has arisen from the primitive idea that no one need die unless an enemy kills him. Of course there are occasional cases relating to debts, and also to wives, slaves, or other property (and also to disputes regarding antelope, hippopotami, and other large game wounded by one person and killed or found dead by another) which do not fall under these headings, although such disputes are often settled by village chiefs. In the case of failure to agree on a decision the parties as a rule go first to a witch-doctor and attempt to settle their claims by divination. The systems of divination (called variously "Taha," "Ongombo," "Ongiki," etc.) are of great interest, but their consideration lies without the scope of this paper. If divination fails the aggrieved party then challenges his antagonist to the ordeal of poison, a refusal to meet which is tantamount to a confession of guilt.

Methods of Conducting the Ordeal.—The first preliminary after the test has been agreed to is to decide upon a witch-doctor who is acceptable to both parties to prepare the poison. Then each party ties up and delivers into the hands of a disinterested person a free-born boy or girl as a hostage to insure payment of the penalty (often a fine of cattle or slaves) which will be exacted in case of his death. Now the two companies, consisting of the litigants, their friends, and relatives, proceed, usually by separate routes, to the village of the witch-doctor, who may be several days away, and to whom each party has previously forwarded presents, bribes, and assurances of the sender's innocence. Each man's friends, too, use all their personal influence to win over the witch-doctor. It will be seen by this that it is always decided beforehand who is to be acquitted and who convicted by the ordeal. On the day appointed there is usually a crowd of natives to see the spectacle. The litigants appear, and after each has solemnly asserted his innocence in a long speech, or by oath, drink the poison. There are several methods of administering the test, which I may briefly describe:

1. The first of these is to mix two small gourds full of apparently identical concoctions, each litigant drinking the contents of a gourd. Trickery and suggestion (at both of which savages are experts) are brought into play to place the deadly gourd in the hands of the devoted individual. The imposture is so palpable, however, even to the credulous native, that this method is now almost obsolete, and the demand is usually made that both drink from the same gourd.

2. I have heard of a "one-gourd method," according to which the poisons are mixed and allowed to settle, the person drinking last getting the fatal dregs of the cup.

3. The method which I saw carried out was as follows: The poisonous substances are dried, powdered with various others, and placed in the bottom of a small gourd, where they are carefully covered with the resinous exudation from the "Ulemba" tree (*Ficus psilopoga* Welw.). On top of this is poured an evil-smelling mixture of different harmless solutions. Over the surface of the liquid is sprinkled a light-colored powder. The witch-doctor with many mystic incantations and flourishes stirs the mess a couple of times with his finger, taking care not to touch the bottom. Then the fortunate party whom it is proposed to acquit drinks. The mixture is again stirred, this time scratching the resin at the bottom and liberating the poisonous substances. After a few minutes of ceremonies and rites to gain time for the poison to thoroughly permeate the whole the draught is once more stirred, and the victim (who is always made to drink last) quaffs to his doom.

4. Another method, similar in principle to the foregoing, is to have a skin bag with two compartments, one containing the poisonous powdered substances and the other an innocuous powder of the same color, sprinkling these in turn over the top of an inert mixture.

After the drinking has taken place the witch-doctor gives the command to dance. Drums are beaten, and the litigants dance a native dance, capering back and forth over a space of fifty meters long. Soon the poisoned one shows symptoms of dizziness and falls to the ground, to be carried off by his friends to die or recover, according to the strength of the potion given him. The convicted person's relatives must now pay all the claims of the acquitted,[1] and whole families frequently become slaves in this manner.

The Ingredients Employed.—The plants which are used in various parts of Africa are many. Some of these which have been especially studied are *Strychnos icaja* Baill., *Physostigma venenosum* Balf., *Erythrophlœum judiciale* Proct., *Tanghinia venenifera* Poir, *Adenium somalense* Poir, and *Menabea venenata* Baill. None of these plants are used in the poison test of the Umbundus. The principal ingredient is, however, an *Erythrophlœum* (*E. guineense* Don.), which may be combined with either or both of two other poisonous plants, viz., the "Utata" bush (*Securidaca longipedunculata* Fres.) and, more rarely, the "Okalembe" bush (*Tephrosia vogelii* Hook. fil.).[2] I was once told that the "Ochimbinga" plant (*Strophanthus sp.*), formerly employed to poison arrow heads, is also used, but later inquiries failed to corroborate this statement. Several *Ebenaceæ* were also once pointed out to me in the same connection. Perhaps a remark on each of the three most used substances may be in place. Technical descriptions of the plants are not given, as they may be easily looked up in the published systematic books and papers of Oliver, Welwitsch, Ficalho, and others.

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[1] In case the accused is acquitted he insists on the payment of an "Ombalu"—*i.e.,* indemnity for being unjustly accused.

[2] Some deny that *T. vogelii* is ever used.

1. *Erythrophlœum guineense* Don. (*Leguminosæ*). Closely related to the type *E. judiciale* Proct., used in many parts of tropical Africa for the same purpose. It is a large tree with rough bark, handsome acacia-like leaves, fragrant flowers, and a rather large, oval, smooth, yellow fruit which, although acrid when green, is sweet and edible when ripe. The bark of the root is used. This bark when powdered and inhaled causes sneezing. The aqueous extract when injected under the skin of animals causes vomiting and shortly irritates, and later paralyzes the vagus nerve, causing the heart to slow and at last to stop. I administered a piece of bark two inches square and one-third inch thick, ground up and mixed with water, to a small native dog. Its limbs were paralyzed in twenty-one minutes, and it died in one hour and two minutes.

2. *Securidaca longipedunculata* Fres. (*Polygalaceæ*). A large shrub with small fleshy leaves and rose-colored flowers. The inner bark of the root contains an active poison. I prepared four grammes of this bark by boiling in 30 Cc. of water and gave it to a large female mandril (*Cynocephalus sp.*), called "Epundu." It produced death in forty-eight minutes. The roots are often used by the native women to

commit suicide. The method as described by them consists in placing small quantities in the nostrils, ears, armpits, and vagina; but in the only case which fell under my notice an emetic brought up generous quantities of the drug from the stomach. The roots when cut or bruised give off a strong odor of *Oleum gaultheriæ.*

3. *Tephrosia vogelii* Hook. fil. (*Leguminosæ*). A small shrub cultivated in fields or villages by fishermen. I have not tested this plant, but a few handfuls of the leaves bruised and thrown into a small stream stupefy or kill all the fish for a long distance down stream. The plant is also sometimes mixed with food and employed to kill enemies.

Effects of the Poison Test.—As has been said, a number of inert substances are invariably mixed with the poisons. The effects of the general mess as administered are first vomiting and purging. Later the limbs seem to be affected, and the victim falls to the ground, and dies with apparently little suffering. Various glucosides, alkaloids, etc., prepared from poison-test ingredients have been studied. Erythrophlein, the active principle of the chief ingredient of the test under discussion, has been experimentally shown to produce dyspnea, vomiting, diarrhea, slowing of the heart's action, suffocation, and death. It will have been noticed that all of the methods of administering the "Ombulungu" are open to error, and accidents involving either the "innocent" party alone, or even both partakers, undoubtedly occur.

OBSERVATIONS.

The psychological and evolutionary aspects of the custom would repay study, but only a few general remarks can be included here. The natives when questioned attribute the decision to "Suku" (God or chief spirit), but believe that the "Olosande" and "Ahamba" (good and evil spirits or angels) have an influence, and offerings are made to these before going to the ordeal. Offerings are never made to "Suku," as he is conceived only as the creator who has handed the affairs of the world of men over to the "Olosande," "Ahamba," etc., and is only to be approached through these. When pressed as to the matter of deception the natives take refuge in the familiar and unassailable theological position that even the trickery and deceit may be controlled by the spirits. The custom must be (judging from its elaborate ceremonies, traditions, etc.) an old one. Just how it arose and the circumstances of its introduction into Angola are interesting problems. It should be sternly put down by administrators and not winked at, even though, as is now often the case in Angola, modifications (the most common of which is probably the omission of the most dangerous ingredient, *Erythrophlœum*) are adopted in order that it be not invariably fatal.

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SOME ETIOLOGICAL SUGGESTIONS.*

(1) CONCERNING THE SIGNIFICANCE OF AN EMBRYO INTESTINAL WORM FOUND IN THE BLOOD STREAM; (2) REGARDING A SPIROCHAETE FOUND IN YAWS PAPULES; AND (3) A HINT AS TO THE POSSIBLE CONNECTION BETWEEN CHIGGERS AND AINHUM.

BY F. C. WELLMAN, M.D. BENGUELLA, ANGOLA, AFRICA.

I.

THE fact that the following suggestions may possibly have an immediate bearing on the etiology of several tropical affections has led to their publication in this incomplete form.

In my last report on the disease incidence of my district in West Africa I figured and described an unknown entozoal embryo found in the blood stream of a young negress. It was differerent from the so-called *Anguillula stercoralis* and from the embryo of *Uncinaria duodenalis*. Its presence in the circulation puzzled me, although I referred at the time to Looss's work with larva of *U. duodenalis* as indicating a possible explanation of the presence in the blood of the worm seen by me. My exact words on this point were as follows: "That the embryos of at least some entozoa can pierce the tissues of their host is proven by the experiments of Professor Looss with the embryos of *A. duodenale* in Egypt, some of whose preparations I have seen. Bentley's work on the etiology of Pani-ghao in Assam proves the same thing."[1] Later researches by Looss show that the larvæ, after piercing the skin, leave the subcutaneous tissue in the blood stream, and, passing through the right heart to the lungs, travel up the trachea and down the esophagus to the stomach and intestines. These researches having been fully confirmed by the later work of Schaudinn, Smith, Lambinet, Herman, Boycott and others,[2] it has occurred to me that my worm may be the larval form of some other intestinal parasite which when observed was in the process of reaching by a similar route its normal habitat in the alimentary canal. If it should prove to be the case that intestinal worms other than *U. duodenalis* may enter their host through the skin, the proneness of barefooted and scantily clothed races to helminthiasis would receive additional explanation and a definite means of prophylaxis would be suggested.

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II.

Some time ago while examining a scraping from a yaws papule, I was somewhat surprised to see under the 1/12 oil-immersion lens a number of active spirilla-like bodies which in form and movement closely resembled *S. obermeieri*. Thinking it to be a case of the parasite of relapsing fever I thereupon made a prolonged and careful examination of the blood which, however, contained no spirochaetes. I found the parasites in other papules of the same case. The patient, a young girl probably alarmed at my interest in the case, promptly decamped. Having never demonstrated this parasite in cases of yaws examined before or since I concluded that its appearance in this case was accidental, and connected it with similar organisms which have been described in *Pyorrhea alveolaris* and other chronic inflammations of the mouth and different parts of the body. In thinking over the matter since, in the light of Schaudinn's announcement that the *Spirochaeta pallida* is the germ of syphilis (which seems to be confirmed, or at least it seems to be proved that that parasite is found only in the lesions of syphilis — by such high authorities as Metchnikoff, Fränkel and Lehman), I have wondered if the spirochaete seen by me in yaws may not, after all, be significant. The many points of likeness between yaws and syphilis (which has led to theories of their actual identity as held by Hutchinson, Scheube and others) lends weight to such an idea. Of course a single observation is of no great value. However, there may be reasons why the parasites cannot be found at all times during the disease, and we know that such organisms stain badly. I hope to make further observations on the subject and hope others will do the same. If such *spirochaetæ* as I have mentioned be related, as Schaudinn maintains, to the trypanosomes a suggestive parallel is seen in dourin, a trypanosome affection of animals which is transmitted by coitus. Wright has pointed out[3] that the lesions in dourin and those seen in the mouth associated with the presence of spirochaetes are very similar. I have never been (on clinical grounds alone) a friend to the actual identification of yaws with syphilis. Their histo-pathology has, however, many points in common, and, should the germ of both turn out to be a spirochaete or trypanosome their relation could be regarded as even closer.

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[1] *Vide* report published in the New York and Philadelphia Medical Journal, Aug. and Sept., 1905.

[2] *Cf.* Boycott, Journal of Hygiene, v. 3, p. 283.

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[3] Lancet, July 9, 1904, p. 74.

In such an event the venereal disease of horses and two of the great venereal diseases of man (syphilis and yaws — which latter is undoubtedly often transmitted by sexual contact) would be shown to have a similar etiology.

III.

Some time ago, while engaged in a study of the chigger (*S. penetrans*) and later during the observation of several cases of ainhum, I noticed that the chigger has, even in healthy feet, a predilection for the under surface of the little toe, and especially so if, as is so often the case, the skin is cut or torn. It is well known to those who have studied the habits of the chigger that the insect invades abraded or irritated surfaces oftener than sound skin. The fold of skin under the proximal joint of the little toe corresponding to the edge of the web between the toes is the point where wounds are oftenest made by the sharp grasses, etc., through which the barefooted native walks and runs. The principal reason for this in the African is that the little toe of barefooted negroes lies separate from the others at an angle due to anatomical reasons connected with flatfootedness. As I have said, chiggers are oftenest found on the under surface of this toe even when all the toes are intact. When wounds are once made here, however, the chiggers persistently invade them and must be removed constantly. While I do not wish to be read as advocating *S. penetrans* as the sole cause of ainhum, it seems to me that these insects must play a part (in some instances, at least) in the continued irritation which, especially in blacks (who have a fibrogenetic tendency), may lead to the contracting fibroses occasionally resulting in the spontaneous amputation known as ainhum. Such a theory goes far to account for the geographical distribution of the disease which is particularly common in the two great homes of the chigger, *viz.*, tropical America and Africa.

The above conjectures which are, I admit, founded on slight evidence are not put forth in a dogmatic spirit but merely in the hope that they may prove suggestive to those working on the etiology of tropical diseases.

SUPPLEMENTARY NOTE ON A SPIROCHAETE FOUND IN YAWS PAPULES. *

BY F. C. WELLMAN, M.D., BENGUELLA, ANGOLA, AFRICA.

SEVERAL weeks ago I sent to Professor McFarland a paper in the course of which I mentioned the fact that I had found *spirochaetae* in the papules of a case of yaws.

Only yesterday there reached me the report of the meeting of the British Medical Association at Leicester. At that meeting Dr. Aldo Castellani announced[1] the discovery of *spirochaetæ* in two cases of yaws in Ceylon. One of his observations dates back as far as February, 1904. My independent discovery of this organism in yaws papules (which may now be regarded as a confirmation of Castellani's previous observation) only dates from July 14, 1905. So I have thought it worth while to publish this additional note which will serve to obviate any misunderstanding that might arise from the tenor of my previous paper which was on its way to America before Castellani's announcement reached me.

It is significant that this observation (which has been spoken of as "one of the most important discoveries of recent times, considering the fact that the *Spirochaeta pallida* has been found by Schaudinn in syphilis, and considering the relation said to exist between yaws and syphilis"[2] should have been made almost simultaneously in two such widely separated countries as Ceylon and West Africa. It is to be hoped that observers in all parts of the tropics will avail themselves of every opportunity to thoroughly investigate the matter.

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* This paper by Dr. F. C. Wellman as received by us Dec. 7, 1905. Owing to a misunderstanding its publication has been delayed.

[1] " On the Presence of *Spirochaetae* in two Cases of Ulcerated Parangi " (Yaws). Abstract in Journal of Tropical Medicine, Aug. 15, 1905, p. 253

I have sent a statement similar to the above to the *Journal of Tropical Medicine*, London.

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[2] Brit. Med. Jour., Aug., 5,1905, p. 282.

EXPERIMENTAL MYASIS IN GOATS, WITH A STUDY OF THE LIFE CYCLE OF THE FLY USED IN THE EXPERIMENT AND A LIST OF SOME SIMILAR NOXIOUS DIPTERA.*

F. C. Wellman, M.D.
(*Benguela, Angola, West Africa.*)

INTRODUCTION. — Myasis, especially in tropical countries, is a not unimportant affection which, by virtue of its oftentimes severe symptoms in such climates, generally attracts the attention of and impresses itself upon the memory of the visiting foreigner. Consequently some of the flies giving rise to the more striking forms of myasis, such as that caused by the Screw-worm, the Ver Macaque, and the Ver du Cayor, have been carefully studied. Other flies noxious in the same or similar respects are, however, comparatively unknown. Especially is this true of some which are found in tropical Africa.

The writer some months ago sent from Portuguese West Africa to America dipterous larvæ which he had extracted from the subcutaneous tissues of a child and a dog, and more recently has reported a case of intestinal myasis due to the larvæ of *Anthomyidæ* of which the life history was described. Following this latter study the experiment here reported was undertaken to determine if another fly with suspicious habits and common in the same region would, under favorable circumstances, produce destructive myasis.

THE FLY STUDIED. — The fly employed was a large, dark fly, which was pronounced by Mr. Austen of the British Museum to be a species of *Sarcophaga* near *regularis*, Wied. It is vivaparous, and I have often seen it depositing its larvæ on decaying meat and feces and, on one occasion, in wounds. The larvæ are small when first deposited (four to five millimeters long), but before pupating reach the length of fourteen millimeters or more. I have neither figured the fly nor

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attempted its description, as I have sent specimens of the larvæ at different stages in their development, as well as of pupa and imago, to Professor McFarland, of Philadelphia, and they will be submitted for determination and description, which description will be published later.

THE SUBJECT OF THE EXPERIMENT. — The animal used in the experiment was one of the native goats of Angola. This animal was chosen as being tame and easy to operate upon, and also because it is not known to suffer here from myasis in its natural state.

METHOD OF PROCEDURE. — The method adopted was as follows: A large number of the flies (seventy) were caught in an improvised fly trap baited with decaying meat. The goat was chloroformed and placed under a mosquito curtain, and tied in such a manner that it could not move its head or otherwise protect itself from flies. Then the edges of its nostrils were painted with water in which had been macerated pieces of putrid meat, and the flies liberated under the curtain. The flies could be seen entering the nostrils (which had been previously examined with a speculum, and were known to be in a healthy condition and to contain no maggots) from time to time. The goat was untied at the end of one hour, and confined where it could be watched.

CONTROL EXPERIMENT. — Two other goats had their nostrils painted at the same time with the baiting mixture, but were not confined with the flies.

RESULT. — The goat seemed to experience little discomfort from the time of the experiment (3 P.M.) until the next morning, although it could be heard sneezing in the night. The following morning, however, it would not eat and was thirsty, feverish, and seemingly in pain, as it bleated constantly. The odor from the nostrils was extremely fetid, although the maggots could not be seen on external examination. By evening it was very ill and would not stand up. It was killed on the morning of the third day, and a post-mortem examination made at once.

POST–MORTEM EXAMINATION. — The post-mortem findings were as follows: The anterior nares were unaffected. The posterior nares and the frontal sinuses were extensively eroded and of a dark red color, in some places almost purple. In no instance were the erosions deep enough to involve the bone or even the periosteum. The maggots themselves were plentiful throughout the frontal sinuses and posterior nares, in some places being packed together in writhing masses. I only found two in the pharynx. None were found in the trachea, bronchi, esophagus or stomach. The eustachean tubes, too, were free. In all, one hundred and thirty-eight maggots were turned out, most of them of nearly full size. The air passages of the goat contained a thin, glairy pus with a markedly foul smell.

INTERPRETATION OF THE EXPERIMENT. — The severe inflammation and necrosis was probably entirely due to the presence of the flies and their larvæ and not to infection through the putrid meat juice used to attract the flies. This would appear from the fact that there were no lesions whatever in the anterior nares, and also from the fact that the two animals (treated identically but not exposed to flies) used as controls developed no symptoms whatever.

LIFE HISTORY OF THE FLY. — The maggots were compared with specimens which I had on a previous occasion bred from the same kind of fly, using feces as food for the larvæ, and seemed to be identical. I, however, after dropping a few into a weak formalin solution to keep as types, divided the remainder into three lots. One of these I placed in dry sand under wire netting; the second was placed on fresh feces similarly protected, and the remainder in a third cage in a dish of putrid meat. The first lot pupated in twelve hours, but the puparia were smaller than normal, of a lighter color (reddish brown) and of a different shape from the others, being more pointed at the ends. These did not produce imagines although kept for over a month.* The second lot on feces pupated in eighteen to twenty-four hours, the puparia being larger, plumper, of a dark brown color, and blunter at the ends. Imagines emerged from the puparia in twelve to thirteen days which were of full size and identical with those secured for the experiment. The third lot on putrid meat pupated in twenty-eight to thirty-six hours, the pupæ being larger, darker, and better formed than those of Lot 1, but not so regular as those of Lot 2. Some of them (about two-thirds) produced imagines in twelve to fourteen days. These were identical with the others except that they were somewhat irregular in size and on the whole rather smaller than Lot 2. From this it would appear that feces is the normal habitat of the larvæ. I shall not, as I have said, give here measurements, or attempt description of the larva, pupa, or adult fly, since this will be done later by an expert systematist more able than I can hope to do.

CONCLUSION. — It would seem fair to conclude in view of the above experiment that men and animals might be invaded by the fly in question under certain circumstances. I should consider sleeping here in the open, especially by any one with ozena, or fetid breath from any other cause, to be dangerous. Uncovered wounds are also, as I have myself proven, liable to invasion by this fly.

ALLIED NOXIOUS DIPTERA. — Finally, I give a list of some allied flies that have been convicted of causing human myasis in one form or another. It will be seen from a study of this list that myasis of different sorts is far from being a negligible factor not only in tropical but also in general pathology. The classification followed is that of Brauer:

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* A few (ten per cent) of this lot of pupæ produced imagines after this paper was written. They were smaller even than those from Lot 3.

DIPTERA.

Clyclorrapha — Schizophova — Muscidæ — Calyptratæ.

Oestridæ:

Gastrophilus. *G. equi* is the well known bot-fly of horses, etc. The young larvæ are said to also infest man, boring into the epidermis.

Hypoderma. *H. bovis* has been known to invade man. The eggs are laid on the skin, and the skin and the larvæ bore into the epithelium causing swellings. Three cases of *H. diana,* which infests deer in the same manner, have also been observed in man.

Dermatobia. The larvæ of *D. cyaniventris* is the "Ver Macaque" of tropical America, and in man causes painful boils, occasionally attacking the eyes. A number of vague reports from Africa of flies, the larvæ of which cause boils in man and animals, have been published, and, although the imagines have not been obtained, the habits of these would seem to be much like those of *D. cyaniventris.* Scheube has collected a number of these instances from German East Africa, Tanga, British East Africa, the Transvaal, and Lake Nyassa. Strachan mentions a similar fly in Lagos, and the writer has reported cutaneous myasis of a similar character in Portuguese West Africa. Scheube also mentions a very small fly from Guatamala and other flies from the Shetland Islands and Norway, which give rise to similar conditions. This latter is probably *Hypoderma bovis.*

Sarcophagidæ:

Sarcophaga. Various species of *Sarcophaga* occasionally deposit their larvæ in wounds of man. Those of *S. carnaria* have also been found in the nose, conjunctivæ, ear, anus, vagina, and intestines, as well as in abscesses. *S. magnifica* has been observed to cause abscesses and sinuses after the manner of *Compsomyia macellaria* (q. v.). *S. ruficornis* is one of the flies producing severe forms of myasis in India. A species of this genus (*S. sp.* near *regularis*) is the fly used in the experiment detailed in this paper.

Sarcophila. The females of some species of this genus deposit their living larvæ in the wounds of man and animals. One species in Russia originates disturbances similar to those set up by *Compsomyia macellaria* (q. v.).

Auchmeromyia. The remarkable larva of a species of this fly (*A. luteola*), which was first described by Dutton, Todd, and Christy, is armed with blood-sucking mouth parts, and lives principally on human blood. It is common in Angola and the writer proposes to publish shortly a study of its complete life history. Another species (*A. depressa*) causes cutaneous myasis in Natal.

Ochromyia. The larva of *O. anthropophaga* is the "Ver du Cayor," which in Senegal produces cutaneous inflammation and swelling.

Muscidæ:

Musca. Larvæ of *Musca sps.* occasionally are passed in feces or found in wounds. In this part of West Africa they are largely responsible for the spread of an acute muco-purulent conjunctivitis very common among children, and which sometimes leads to ulceration of the cornea and blindness.

Calliphora. Larvæ of different species have been found in intestines of man and animals.

Compsomyia. The larva of *C. macellaria* is the "Screw-worm" of tropical America. The parent lays her eggs in wounds and in the ears, nose, or mouth of any one sleeping in the open. The larvæ burrow in the tissues, causing grave symptoms and not seldom death. The same or a very similar fly has also been observed in Cochin China, Tonquin, and India.

Lucilia. *L. sericata* is the cause of "maggot" in sheep. The larvæ of several species of *Lucilia* have been detected in wounds and ulcers in man and animals. Braun cites a case of the larvæ of *L. nobilis* being found in the suppurating ear of a man in Denmark, who had slept in the open air. There are several species of this genus, one at least of which is new, in the region where this paper is written.

Anthomyidæ:

Anthomyia. The larvæ of *A. canicularis* not seldom get into the stomach and intestines of man, through eating raw vegetables, where they set up severe disturbances until vomited or passed. The writer has recently published a case of intestinal myasis produced by *Anthomyidæ*, in which diarrhea, fever, and severe abdominal pains were observed.

Hydrotæa. The larvæ form has been found in the feces of human beings.

Homalomyia. The larvæ have often occurred in the intestines of man, being passed alive in the feces. Osler gives a case of infection by *H. Scalaris* in Louisiana. The writer has discovered larvæ of unknown flies in freshly voided feces of West African negroes.

Hylemyia. Larvæ of these flies have also been passed in human excreta. In the district where this paper was prepared there occur several species of *Hylemyia*, among which may be mentioned *H. fasciata* and a new species not yet described.

This list is by no means exhaustive, only a few books and no recent periodical literature for several months back being available in the place where this is written. A number of flies indefinitely reported have, too, been omitted. Braun mentions *Phora rufipes*, *Piophila casei* and *Teichomyza fusca* as each having been passed in the feces of man. The last is probably not uncommon. Theobald speaks of the probability of *Cynomyiæ* laying their eggs in wounds. The possibility of flies which molest animals (such as *Hypoderma lineata* in the case of cattle, *Oestrus bovis* in sheep, *Cephalomyia maculata* in camels, and *Cephenomyia rufibarbis* in deer) also infesting man should always be kept in mind in investigations of this kind.

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NOTE.

DECEMBER 1, 1905.

DEAR DOCTOR: I have your letter of the 27th, and the specimens and manuscript from Dr. Wellman. I have read the manuscript with interest, and return it and the specimens herewith. The determinations of the material by my expert assistant in Diptera, Mr. D. W. Coquillett, are as follows:

No. 538A.

Lot 1. Probably *Sarcophaga Africa*, Wied.

Lot 2. *Sarcophaga Africa*, Wied (described from Africa). 1824: Analecta Entomolog., p. 49, No. 103.

Lot 3. *Sarcophaga albofasciata*, Macq. 1851: Diptera Exotiques, p. 205 (described from Africa).

Probably *Sarcophagid* larvæ.

Yours most truly,

L. O. HOWARD,

Chief of Bureau.

Dr. JOSEPH MCFARLAND.

Reprinted from the New York Medical Journal for June 23, 1906.

BITE OF THE OMBUTA (*CLOTHO ARIETANS,* GRAY), TREATED WITH POTASSIUM PERMANGANATE. RECOVERY.

By F. C. WELLMAN, M. D.,

ANGOLA, WEST AFRICA.

(Published Under the Imprimatur of the American Society of Tropical Medicine.)

In view of recent reports from India and elsewhere of experiences with the method of treating snake bites mentioned in the title of this paper, the following notes on a case occurring in West Africa may be of interest:

Case.—A male negro, of the Chiyaka tribe (Bantu), twenty years of age, was bitten in the foot about half an hour before I saw him (3:25 p. m.) by an ombuta while felling a tree in the bush. He at once tied a piece of bark string tightly about his ankle and came with all haste to the "white doctor," who happened to be in the vicinity.

Status præsens.—The patient is howling with pain and all the natives about say he will die. On the dorsum of the foot are the marks of the snake's fangs. They consist of two tiny parallel gashes about three millimetres in length. Considerable swelling is already seen in the foot, which also feels hot and dry. The patient says he is very thirsty. A thin, bloody fluid, which when tested shows an acid reaction, slowly exudes from the wound. Temperature, 99.8° F.; pulse, 92; respiration, 28.

Treatment.—I immediately excised the bitten place and dissected out a fair sized piece of the subcutaneous tissue beneath. The wound thus made was filled with crystals of pure potassium permanganate and an aqueous solution of the same injected with a Pravaz

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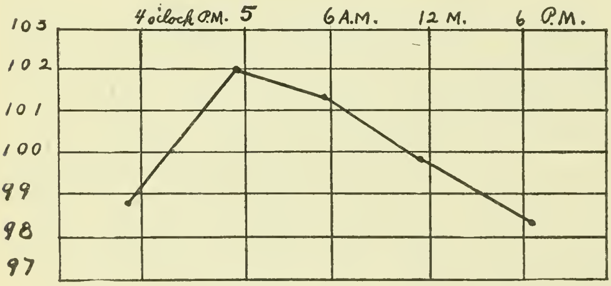
syringe into the surrounding tissues. A piece of bichloride gauze was then applied and the foot loosely bandaged. The patient was well alcoholized, but no other internal treatment was given.

The leg continued to swell and the œdema soon reached to the knee, making it difficult for the patient to move his ankle. The wound oozed blood which seemed to lose, while passing through the tissues adjacent to the bite, its normal coagulating power, although the finger blood tested by Wright's method coagulated in about eight and a half minutes. I did not spectroscope the blood oozing from the wound, but the bright red color was strikingly different from the dark sepia color seen in some cases of snake bite and suggested the appearance seen when carbooxyhæmoglobin or cyahæmoglobin are present. Hæmoglobin (Gowers) estimated at 70 per cent.; red cells (Thoma-Zeiss), 4,500,000; leucocytes, 7,400. Blood slightly alkaline in reaction by Haycraft-Williamson method. After about an hour the patient began to vomit first food and later a bloody mixture. The temperature in the mean time had risen to 102° F. I thereupon made some microscopical examination of his blood, and three hours later found small malarial parasites (*Hæmomenas præcox*, Lav.). The red cells seemed unchanged by the poison, and the leucocytes normal. During the night the patient had a violent attack of epistaxis;[1] and later stated



Temperature chart of case.

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[1] The coagulability of his blood was found on retesting to be practically unchanged.

that he had not slept on account of the pain in his leg.

The swelling the next morning was about the same as when I had last seen it at 9 o'clock the previous evening; temperature, 101.4° F. A peculiar jerky respiration with a sighing expiratory effort was also noticed. On examination the wound was found at this time to consist of a smallish, gray slough which spread rapidly for the next two days until it involved about half of the dorsum of the foot, exposing the sheaths of the tendons and other deep structures. The bones were not affected. The temperature fell to normal on the second day in the midst of this sloughing process. At the end of a week the slough was largely thrown off and satisfactory granulations appeared. The patient made an uninterrupted recovery, coming back two months later to show me the scar where the foot had healed.

The Snake.—Clotho arietans, Gray. Synonyms. *Bitis arietans, Vipera arietans,* eliuta, ombuta, liliuta (Bantu names), puff adder, cobra do matto. The snake, rather badly mutilated, was brought to me, having been killed in a brush heap at the spot where the victim had been working. It measured 102 centimetres in length, and proved to be the well known and justly dreaded *Clotha arietans* of South Africa. The natives are very much afraid of this snake, and tell many stories of people who have died from the effects of its bite. The case above reported is the only one which I have had the opportunity of carefully studying. There are several poisonous snakes in this district and many others concerning which fabulous stories are told. One of the most dreaded snakes, called by the blacks ohakati, I have not seen, but the descriptions given of it by natives and colonists seem to point to a horned viper similar in size and appearance to *Viper cerastes.* Native reports of snake bites are utterly untrustworthy.

Remarks.—Some points of interest in the above case are:

1. The loss of the coagulability of the blood after passing through the tissues at the seat of the bite.

2. The vomiting of blood (which, however, may have been due to violent retching) possibly from

extravasation from the coats of the stomach. Such extravasations are attributed to the direct action of a special constituent of snake venom more abundant in the poison of the *Viperidæ* than in colubrine snakes.

3. The violent epistaxis.

4. The remote selective action of some ingredient in the venom noticed by its effect on the respiration.

5. The sloughing of the site of the puncture which cannot be attributed to the permanganate as it is a common feature in snake wounds.

6. The stirring up of a latent malarial infection and the finding of parasites in the blood.

7. The complete recovery.

Following are a few references which are available here and which I have examined for the sake of comparing my case with others:

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Reprinted from the New York Medical Journal for March 31, 1906.

REPORT ON THE INSANITARY CONDITION OF VARIOUS TOWNS IN THE COLONY OF ANGOLA.*

By F. CREIGHTON WELLMAN, M. D.,

ANGOLA, WEST AFRICA.

The phrase "fifty years behind the times" and similar sayings are not uncommon when speaking of ignorant or conservative communities. The following facts concerning the conditions obtaining in Portuguese West Africa may possibly tempt the reader to search for a stronger expression. In the colony under consideration there exists an almost entire absence of any of the provisions with which sanitary science has furnished us for protecting the lives and health of human beings living in close proximity. I can probably best illustrate this statement by taking as a type of the Portuguese West African town the city of Catumbella, with which I am perhaps best acquainted. This town lies about sixteen miles from the sea coast and is the first station of the new railway now being built from Lobito Bay to the interior via Benguella and Caconda. I shall take up in order its water supply, the disposal of excreta, the dust question, drainage, irrigation, swamps, and mosquitoes, touching briefly upon each of these points and then in a few words extending my remarks to other towns and cities of the colony.

Water supply.—The water for the city is drawn from the Catumbella river. There is a pumping station on the banks of the river a little distance above the town. The water is simply run to the station and then pumped into the town. No attempts at settling, filtration or other methods of

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purification are made. Much of that part of the town near the river receives its water direct from the stream by means of water carriers. The water is muddy, flat tasting and bad smelling. It is generally filtered through " Mossamades stone " before drinking, but the stone is so porous that bacteria undoubtedly pass, and except for the possible removal of the ova of entozoa no advantage is gained save in the appearance of the water. On the banks of the river above the pumping station at a point called Esupua are the permanent camping places of the thousands of native rubber, ivory, and slave traders, and porters who are constantly coming and going between the coast and the interior, hundreds of them arriving in Catumbella every day. I have spent the night at Esupua, which is the last camp before reaching Catumbella when coming from the interior. Not caring to occupy all the space placed by the editor at my disposal with an enumeration of the sights and smells of one locality, I shall leave the condition of Esupua (which is under no supervision whatever) to my reader's imagination, contenting myself with stating that one must be careful in venturing out of camp to avoid stepping in fæces, and that on one occasion I saw there three dead bodies of slaves who had perished on the march, lying by the side of the river. I should also mention, before passing to my next point, that the natives are allowed to bathe where they please, and I have seen them bathing at a point in the river just above the pumping station.

Disposal of excreta.—I have used this conventional term which is something of a misnomer here, unless permitting defæcation on the edges of the town, in the streets or even in the compounds of the trading houses may be properly designated as " disposal." The European part of the town defæcates in " basios," which are tall metal, granite ware pots which may be emptied every day or only when full, according to the taste of the owner. At any time of the day, but generally in the evening, one may if his nose allow him to venture into any of the by-streets, meet with these pots on the heads of slaves (who are always spoken of, in deference to the Berlin Treaty, as contract servants), being carried to the place of disposal. The place of disposal seems to be almost any situation, but generally the edges of the town and near the river. As to the native fixed and transient population no provision whatever is made for them. There is not, so far as I know, a latrine of any kind in the town. In the day time the blacks seem to prefer the slopes above the town on the sides of the hills (Catumbella lies in a narrow valley with the hills almost within stone's throw of the principal streets), but at night they never go so far. After dark they use the back and even the main streets and sometimes, as I have mentioned, the compounds in which they sleep. In order to urinate no one, white or black, seems to think of retiring either from the public view or proximity to the main buildings of the town. I have more than once watched a white man stand in the door of his place of business and urinate into the street. The result of all this is, not to mention smells again, hordes of different sorts of flies (principally *sarcophagidæ* and *anthomyidæ*, both of which I have demonstrated to be the cause of some terrible forms of myasis occasionally seen here) and other evils too numerous to specify.

Dust and drainage.—In the dry season each slight wind raises a natural cloud of dust, and in the early morning the long suffering visitor, who has unwillingly arisen early and repaired to the upper veranda to escape the intolerable heat of his bedroom, has his nostrils greeted by an extra and artificial cloud of the same dust raised by the women who sweep the dry streets with twig brooms. In the wet season floods of water sweep down from the hills bearing on their bosom the pollution accumulated during months of the processes described under the preceding heading. Mosquitoes flourish in great numbers from pools caused by rain (the town site is very flat), the waste from the native water tap, and the swamps and irrigation ditches about to be mentioned. In some seasons I have been forced, when in Catumbella, to have a mosquito curtain arranged over my bath in order to enjoy my tub in comfort.

IRRIGATION SWAMPS AND MOSQUITOES.—Irrigation is allowed without any restrictions or supervision. A large rum plantation lies on the very edge of the town site. Swamps receive no attention whatever and the banks of the slow flowing river are left to their own devices. Mosquitoes, among which I have noticed two different *Anopheletes, Myzomyia funesta, Celliæ* and a species of *Pyreptophorus* (*? Austeni*) not to mention *Culicides*—abound throughout the year. I have no statistics as to the disease incidence of the place, but the town has an evil reputation for pernicious malarial attacks and black water fever.

I have not spoken in this report of the neglect of undergrowth near the river, the allowing of native quarters in the closest proximity to the European, the poor ventilation afforded by the style of house preferred by the Portuguese, the arrangements for killing animals, the typical Portuguese hospitability and personal habits, as well as various other points of comparative insignificance beside the fearful general conditions tolerated throughout the city. The foregoing remarks apply more or less to the other towns and cities in this colony which I have visited and which include the cities of Loanda and Benguella, the ports of Ambriz, Landana, and Novo Redondo, besides the interior towns of Malange, Lucalla, and Quissol. The amazing ignorance and apathy of the Portuguese government and people in allowing important points, which might be made healthy and prosperous, to remain "death holes" like Catumbella, seems almost incredible in this age of sanitary progress and general education.

Extracted from the American Journal of the Medical Sciences, May, 1906

STUDIES IN TROPICAL MEDICINE.[1]

By F. Creighton Wellman, M.D.,
BENGUELLA, PORTUGUESE WEST AFRICA.

THE CHIGGER IN SOUTHWEST AFRICA.

INTRODUCTION.

The chigger, chigoe, or sand flea (to mention but a few of its common names) receives, as a rule, but slight attention at the hands of writers on tropical diseases, and is often dismissed with little more than a passing mention. The animal, however, merits more consideration than it generally receives, as it not seldom plays no insignificant role in the production of mutilation and disease. The insect is a common pest throughout the colony of Angola and is especially abundant in the district of Bailundo, where the writer is stationed. It is believed that a few notes concerning its occurrence in this part of the world may not be without interest.

NAMES AND SYNONYMS.

Pulex penetrans, Linné; *Sarcopsylla penetrans,* Westwood; *Rhynchoprion penetrans,* Oken; *Dermatophilus penetrans,* Guérin; Chigger, Jigger, Chigoe, Chego, Chigue, Chique, Tschike, Djiga (Congo), Sikke (Guiana), Bicho, Tunga, Jutecuba, Migor (Brazil), Nigua (Mexico), Picque (Paraguay) Ewundu (Bailundo), Ochitakaya (Bihé), Katomba (Lovale). The scientific name most generally recognized is S. *penetrans.* The common name for it in this region is Ewundu.

HISTORY OF S. PENETRANS IN ANGOLA.

The chigger was brought into this colony by the Portuguese over thirty years ago (1872). It was first introduced into Ambriz, but soon spread over the entire colony. This was the beginning of its history in Africa. Since then it has traversed the continent, and is steadily pursuing its way around the world. It has already reached Madagascar, and has been reported from India (Bombay) and even from Penang and China, having probably been carried to the far east by Indian coolies returning from East Africa.

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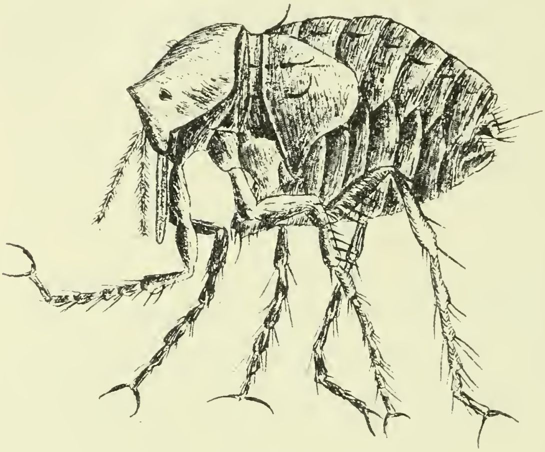
[1] Published under the imprimatur of the American Society of Tropical Medicine.

FIG. 1



Sarcopsylla penetrans, L. ♀ (magnified).

PLACE OF THE INSECT IN NATURE.

S. penetrans falls under the sub-family *Sarcopsyllina,* family *Pulicidæ,* belonging to the sub-order *Aphaniptera,* order *Diptera,* of the class *Arthropoda* in the animal kingdom.

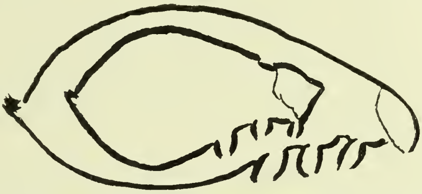
ANATOMY.

Fleas are known from other *diptera* by their laterally compressed body, and by having, in place of wings, two lateral, plate-like appendages on the mesothorax and metathorax. The head is small and not distinctly separated from the body. The antennæ are short and placed in fossæ behind the ocelli. Ocelli may be absent. Mouthparts formed for piercing. The three thoracic and nine abdominal segments are each distinct. Legs modified for jumping. All the known species are parasitic. The genus *Sarcopsylla* is characterized by having the head angular, eyes small, and maxillæ short with epipharynx elongated. In *S. penetrans* the body is decidedly smaller than that of the common flea (*P. irritans*) and it differs somewhat from that insect in shape, the abdomen being wider and the head proportionately larger.

HABITS AND LIFE CYCLE.

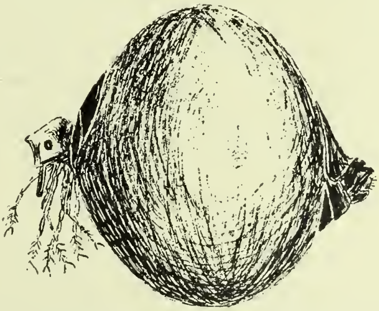
The chigger here lives in the dust, etc., in native kraals and camps. It bites all warm-blooded animals, including man, in the same manner as do ordinary fleas. But if a female be impregnated she takes advantage of her first opportunity to burrow into the tissues of some warm-blooded animal, where she matures her eggs, her abdomen (which admits of enormous distention) swelling during the process to the size of a small pea. There have appeared various accounts of the succeeding steps in the metamorphosis, many of them inaccurate in some points. In books on zoology, pathology, and both tropical and general medicine we read such statements as these:

FIG. 2



Showing the relative size of S. penetrans (the inner figure) and S. irritans (the outer figure).

FIG. 3



Pregnant female chigger, showing distended abdomen.

The eggs are "not deposited while the parasite is in the skin, for the ova do not leave the body until the parent reaches the soil." "The female bores into the skin, and the escaping larvæ give rise to ulcers." "The female lays her eggs in the skin and causes thereby intense inflammation." "After the eggs are laid (according to some, before this process) the superjacent skin ulcerates and the chigger is expelled," etc. During the examination of large numbers of Bantu men I have made the following observations on this stage in the life history:

1. *The eggs are always laid while the chigger is yet embedded in the flesh of her host.*[1]

2. *They never hatch into larvæ in the body of the parent.*

3. They are not laid at one time in masses, but discretely, and sometimes at considerable intervals. The time and rapidity with which they escape depends on the position of the parent and the activity of the host. If the chiggers are in the sole of the foot, and the infected person moves about, the eggs may be seen dropping from his feet as he walks. The pressure on the foot and the action of the muscles assist in the extrusion of the ova. This may be easily demonstrated by slightly pressing the surface of the skin near a ripe chigger, when a few (one to three) eggs will be seen to escape one after another. Such eggs may be placed in a glass-covered dish containing some dust from the floor, and the remaining stages in the metamorphosis watched.

4. After the eggs are extruded they fall into the dust and cracks of the floor or ground, where they hatch into larvæ, pupate, and produce imagines as described by various observers. The shell of the parent when dead and empty of eggs *usually dries up and produces no further trouble.* Occasionally it causes irritation, small swellings, abscesses, and ulcers. If the parent flea is prematurely removed from her burrow under the skin and placed on the ground or in a dish she extrudes all her contained eggs at once and dies, *but such eggs do not hatch into larvæ.* I have tried this experiment a number of times, with always the same result. Even if the chigger is not removed until after her gestation is complete, and she has already begun to lay her eggs, from her position in the tissue only a few of the most mature eggs in the posterior part of the abdomen will develop. Thus, while the burning of all chiggers removed is doubtless a good rule yet it has no effect on the usual mode of propagation, and so long as natives go about with infected feet the cycle will go on.

PATHOLOGICAL IMPORTANCE.

The chigger, while usually producing no serious lesions, cannot be entirely ignored as a promoter of disease and discomfort. I have seen shocking deformities, loss of limbs, blood poisoning, gangrene, and death result directly or indirectly from its presence. I am informed that in the early days here when it was first introduced, and before the natives recognized its evil effects, it caused more havoc than it does now. I can easily believe this, as I have myself noticed more evidences of its effects in the feet of natives over thirty years of age than in younger ones. *Apropos* of the possibility of its being the transmitter of specific micro-organisms, I may mention here that I once found *B. lepræ* in a male chigger, but have not carefully studied the insect to determine if it be in this district a carrier of phytoparasites or zooparasites, etc.

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[1] Her different behavior after artificial removal from the tissues of her host (described later) does not form a real exception to this statement.

ILLUSTRATIVE CASES.

I have collected from my notes the following cases which I give, not as typical cases of chigger invasion, for, as I have said, the condition if attended to gives rise to untoward results, but as extreme instances showing the possibilities of the presence of these pests if neglected or improperly treated.

Case I.—Nakafalatala. Woman, aged sixty years. Good health. chigger entered her great toe and swelled up. She had a small girl dig it out with what was doubtless a dirty knife (as all their knives are). The toe inflamed, and a little pus gathered at the site from whence the chigger had been removed. In a few days gangrene of the toe suddenly set in. The woman (being a bush native) refused to undergo any surgical procedure whatever. The gangrene rapidly spread, and she died in a fortnight from the time the chigger was removed.

Case II.—Mutango. Slave woman, aged thirty-five years, with complete paraplegia from traumatic cause. Hands and feet almost filled with chiggers when I saw her. Many on elbows, hands, and knees. Some on shins, back, sides of mouth, vulva, abdomen, and nipples. She died within a month after I saw her, the chiggers undoubtedly playing a part in the anæmia and general inanition which carried her off.

Case III.—Sekulu. Man, aged forty-five years. The integument of his feet was practically filled with chiggers, some occurring as high up as his ankles. A few were seen on his knees, hands, and elbows. I removed twenty-three from a spot one inch square on the sole of his left foot. This man could hardly walk.

Case IV.—Umbombo. Man, aged thirty years. When a child he cried and made a great commotion if chiggers were removed, so his parents allowed them to remain in his toes. As a consequence he walked on his heels until the calf muscles were atrophied and the flexor muscles of the foot hypertrophied, causing misshapen legs and a permanent hobbling walk. The toes are small, and two are wanting on one foot and one on the other.

Case V.—Kangende. Man, aged twenty-five years. A number of chiggers bored under nail of right great toe, permitting infection, severe inflammation, sloughing, exposure of the bone, and making it necessary to amputate the toe. The result, of course, is a permanent limp.

Other cases might be cited of natives who had lost toes and in other ways become permanently mutilated or disabled from the effects of chiggers, but the foregoing will suffice for our purpose.

TREATMENT OF THE LESIONS.

The chiggers should be removed with a clean, *dull* knife as soon as they are noticed in the skin. In case the tissues are injured in the process some strong bactericide should be applied. All infected lesions should be laid open and thoroughly cleansed. It is occasionally necessary to remove toe-nails in order to accomplish this.

PROPHYLAXIS.

With whites, high shoes and finely woven stockings are the best protection. Native children who are generally infected should be kept away from the European quarters. Native servants noticed with encysted chiggers should be compelled to remove them. Animals should not be sheltered near dwellings. In the dry season sprinkling the floors with kerosene and napthol will prevent chiggers from entering the house.

INTESTINAL MYASIS ACCOMPANIED BY SEVERE ABDOMINAL PAIN, FEVER, AND DIARRHŒA.

Myasis, intestinal and cutaneous, is not an uncommon condition in West Africa. Several months ago I sent from Angola some parasitic dipterous larvæ from the subcutaneous tissue of man and dogs (the imagines of which I was unable to secure) to the Secretary of the American Society of Tropical Medicine, and recently I have had the opportunity of carefully studying a case in which larvæ of a fly (*Anthomyinæ gen et sp. incert.*) were passed *per rectum*.

Following are some notes on the symptoms and the maggots producing them.

No. of Case, F. 938. *Name*, Kamuimba. *Age*, fourteen. *Sex*, female. *Race*, Bantu.

History. Has suffered from severe abdominal pains, also diarrhœa and fever, for four or five days. The case has been diagnosed as dysentery.

Examination. The child is rather thin. Spleen slightly enlarged. Some tenderness over lower part of abdomen. Liver, heart, and lungs normal. Tongue thickly coated with grayish-yellow fur. Breath foul. Patient evidently in distress and highly nervous. Temperature 103.2 F., pulse 110, respiration 32. Microscopic examination of small specimen of feces brought by patient's mother showed no amœbæ or other entozoa, except a few ova of *Ascaris lumbricoides*, L. Urine normal, color dark straw. Blood examination revealed, after a somewhat extensive search, two small, intracorpuscular schizonts of *Hæmamœba præcox*, L. Blood centrifuged for fifteen minutes and carefully examined showed no flagellates or other foreign bodies present. I did not make a differential leukocyte count. Having given orders for the next stool to be passed into a covered glass vessel, I washed and examined the contents carefully, with the result that I found a living dipterous larva which when dropped into a weak solution of formalin assumed a conical shape, the cephalic end forming the apex. Having once made a collection of the common diptera of this region, I recognized the larva as closely resembling that of one of the numerous dung flies (*Anthomyidæ, Sarcophagidæ*, etc.) of the district.

Treatment. Two large doses of castor oil at intervals of four hours. A half grain of santonin was also administered with the second dose to rid the patient of some remaining round worms.

Result. After the first dose of castor oil the girl passed eighteen maggots, eleven of them alive, and two round worms. After the second dose she passed three more ascarides and twelve dead larvæ. In three days the patient had completely recovered without further treatment; the malaria subsided of itself when the exciting cause was removed.

Note on the Larva Passed. Believing the maggots to be larvæ of *Anthomyinæ*, several species of which I had observed breeding in feces, I allowed some suspected imagines access to plates of feces, which I afterward kept under gauze netting for observation. In one of the plates two kinds of larvæ developed, one being that of the *Anthomyinæ* in question, and the other identical with the larvæ of a species of *Sarcophaga*, the life history of which I have since worked out. It had doubtless visited the feces without my noticing it. In two other plates I found only larvæ of the small fly under discussion. These developed in seven and nine days into pupæ. In two weeks (13 to 15 days) after pupation imagines, identical with those which I had placed on the feces, emerged from the puparia. The larvæ passed in the feces of my patient were also identical in appearance with those bred from the adult flies. I have not here attempted any description of the fly in either of its stages of development, as I have sent specimens of larva, puparium, and imago to America for determination and description. This description when drawn up will be published in these columns.

Observations. 1. Myasis produced by *Anthomyidæ* has been recorded a number of times (Dubois, Wacker, Kohn, Finlayson, Osler, etc.).

2. The most common fly of this family causing intestinal myasis in temperate climates is *Anthomyidæ canicularis*, Meig. The larvæ

of this fly develops in cabbage and other vegetables and thus not seldom reaches the alimentary canal of man, causing grave disturbances until vomited or passed *per rectum* (*vide* Braun, *Die Thierischen Parasiten des Menschen*, p. 349).

3. The case I have just reported was probably infected through eating decayed food, which had been left uncovered. The symptoms were severe enough to suggest careful prophylaxis, which would mainly consist in keeping all cooked food protected from flies.

4. Reports of myasis from Africa have been, as a general rule, very vague, and in all cases an attempt should be made to determine the life history of the flies producing such conditions. Larvæ and imagines, at least, should be secured if possible.

[The specimens forwarded to this country by Dr. Wellman were examined in the Bureau of Entomology of the Department of Agriculture at Washington D. C. Dr. Howard, the chief of the Bureau, reported that they were larvæ puparia and adults of an Anthomyid fly known as *Anthomyidœ desjardensii*, Macq., described from the Isle of France.]

MULTIPLE FIBROIDS APPEARING AT IRREGULAR INTERVALS, EACH APPEARANCE ACCOMPANIED BY FEVER.

The man in whom the condition occurred, Lohoka by name, is about forty years old. He was in my employ as native servant for about a year. During this period he suffered five attacks of fever, each attack being accompanied by the appearance of from three to twelve fibromata, ranging from the size of a split-pea to that of a small thimble. They are sessile, movable, and slightly tender to the touch. On each occasion they came suddenly during the rise of temperature (which never went above 103° F.), but when once established they are permanent. The parts of the body affected are: right hand (both palm and back), forearm, arm, shoulder, and thigh, also chest and *glans penis*. He complained of a more or less constant aching in this arm and penis, but his general health did not seem to be affected. I was able to demonstrate a few small intracorpuscular schizonts of *H. prœcox* on the occasion of his first fever, but not since. He has neither eosinophilia nor an unusual excess of large mononuclear leukocytes. Being puzzled over the case I examined him with unusual care, and believe I have excluded filariasis, trypanosomiasis, presence of intestinal entozoa, and also bilharziosis. I have, moreover, on several occasions stained sections cut from the tumors by Ziel, Gram, and with carbol thionin, but found no organisms in the tissue. The histological picture of the growths is practically identical with that of white fibrous tissue. I have not seen the man for about three months, and know nothing of his history since the above was written.

HUMAN TRYPANOSOMIASIS IN PORTUGUESE SOUTHWEST AFRICA.

I recently published a short note concerning a trypanosome found, after many examinations, in the blood of birds in Southern Angola. In the course of further researches on the subject of trypanosomiasis I found, after having made over four hundred (411) careful examinations of human blood for this purpose, abundant trypanosomes in the circulation of a young Bantu man aged thirty. There were also many trypanosomes in preparations obtained by aspirating the cervical lymphatic glands,which glands were not enlarged and seemed in other respects normal. The man would not consent to lumbar puncture, so I was unfortunately not able to examine the cerebrospinal fluid. About 500 cells counted. The leukocyte count in the case is as follows:

Polymorphonuclears	31 per cent.
Lymphocytes	25 " "
Large mononuclears	24 " "
Transitional	7 " "

A peculiar feature of the case is that there were no symptoms whatever. The temperature was normal. A hæmatocrit of the blood showed about 5,000,000 red cells and 7000 white cells to the cubic millimetre. I have frequently seen as great a proportion of large mononuclear and eosinophile leukocytes as this case shows in West African Bantus enjoying the best of health. The facies and general condition of the man, too, denote health and vigor. A feces examination showed only the presence of a few ova of *A. lumbricoides.* Urine normal.

The carrier of the trypanosome which I have found is doubtless the only tse-tse fly which is found in Southern Angola, viz., *Glossina palpalis wellmani,* which was discovered by the writer, and recently described by Mr. Austin, of the British Museum. It resembles in many of its morphological features *Glossina palpalis,* Robineau-Desvoidy, but differs from that fly in several distinct anatomical details. My patient states that he has frequently spent considerable periods of time in the district infested by *G. palpalis wellmani.*

I propose to publish, at no distant date, a study of the trypanosome above mentioned and its probable carrier, together with the bird trypanosome first found, and a similar avian trypanosome encountered since. In the meantime I write this preliminary note to place on record the fact that human trypanosomiasis in West Africa extends at least as far south as the port of Benguella. This is, so far as I am aware, the first case of this infection reported on the west coast of the Coanza River.

September 14, 1905. Since writing the above I have received word from Mr. W. E. Fay, of Northern Bailundo, that he has confirmed my observations by demonstrating the presence of trypanosomes in the blood of a native of that district who was also suffering from malarial fever. This man has also often been in the fly belt infested by *Glossina palpalis wellmani.*

REFERENCES.

The scant medical literature of the chigger, as found in Africa, available here is appended.

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The American Society of Tropical Medicine.

1908.

The American Society of Tropical Medicine.

Papers Read Before the Society and Published Under Its Auspices.

Volume 3, 1907-1908.

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Articles of Association.

CHARTER.

Be it known that the subscribers, having associated themselves together for the purpose hereinafter mentioned, and being desirous of becoming incorporated agreeably to existing laws of the Commonwealth of Pennsylvania providing for the incorporation and regulation of certain corporations, approved April 29, 1874, and its supplements, do hereby declare and certify that the following are the purposes, objects, articles, and conditions of their said association, for and on which they desire to be incorporated.

I. The name of the corporation shall be: AMERICAN SOCIETY OF TROPICAL MEDICINE.

II. The purpose for which the corporation is formed is to advance the knowledge of tropical diseases by encouraging original research by its members and others; collecting and recording facts ascertained by such researches, and disseminating information thereof by discussion among its members and by the publication of papers read before the society.

III. The corporation is to exist perpetually.

IV. The location of the Secretary's office shall be in the city of Philadelphia.

V. The names and residences of the subscribers hereto are as follows: Thomas H. Fenton, M.D., 1319 Spruce St., Philadelphia; Judson Daland, M.D., 317 South 18th St., Philadelphia; Joseph McFarland, M.D., Medico-Chirurgical College, Philadelphia.

VI. The corporation is to be managed by a Council of five members, and a President and Secretary who shall be ex-officio members of the Council. In addition thereto there shall be annually chosen a Treasurer, two Vice-Presidents, and an Assistant Secretary. The names and residences of those chosen for the first year are: Thomas H. Fenton, M.D., Philadelphia, President; James C. Wilson, M.D., and James M. Anders, M.D., both of Philadelphia.

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VII. The Corporation has no capital stock.

American Society of Tropical Medicine.

BY-LAWS.

Recommended by Council at its meeting, March 20, 1903, and adopted May 25, 1903.

Article I.—The members of the Society shall be of three classes: *Active, Corresponding,* and *Honorary.*

Any regular American physician or scientist interested in the study of tropical diseases shall be eligible for *Active membership.*

Any regular physician or scientist not a resident of the United States, who has contributed to the knowledge of tropical diseases, shall be eligible for *Corresponding membership.*

Any scientist who has made eminent contributions to tropical medicine shall be eligible for *Honorary membership.*

The number of active members shall be limited to 200. Candidates for membership shall be elected until 1904 by the Council, and thereafter by ballot at the annual meeting upon recommendation by the Council.

Article II.—The dues shall be fixed each year by the Council, but shall not be increased beyond $5.00 without approval by the Society at its annual meeting.

The regular dues shall be paid by active members only.

The corresponding and honorary members shall be exempt from dues.

Article III.—The officers shall consist of a President, two Vice-Presidents, a Treasurer, a Secretary, an Assistant Secretary, and a Council of five members. They shall perform the customary duties of such officers.

The Council shall have general supervision of the affairs of the Society, and shall meet from time to time as they determine. The

President and the Secretary shall be ex-officio members of the Council. In 1905 three Councillors shall be elected for two years and two Councillors for one year. Thereafter each Councillor shall be elected for two years. In case of death or resignation of any officer or Councillor of the Society, the Council shall be empowered to fill such vacancy until the next annual meeting.

Article IV.—There shall be an annual meeting and such other scientific or business meetings as the Council shall determine.

The annual meeting shall be known as the business meeting when the election of officers for the ensuing year shall be held, and routine and other business transacted.

Article V.—These By-Laws may be amended by a two-thirds vote of the Society at its annual meeting as suggested by Council, provided such amendment has been offered to the Council one month previously, and recommended by it. Due notice of such contemplated changes to be sent out with the announcement of the annual meeting.

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Communications concerning the Society should be sent to the Secretary, Dr. John M. Swan, Philadelphia Polyclinic, 1818 Lombard Street, Philadelphia.

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1903. Dr. W. H. Forwood, 1425 Euclid Ave., Washington.

1904. Professor Grassi, Rome, Italy.

1903. Dr. John Guiteras, University of Havana, Havana, Cuba.

1904. Dr. Victor G. Heiser, Chief Quarantine Officer, Manila, P. I.

1905. Dr. L. O. Howard, U. S. Department of Agriculture, Washington.

1904. Dr. W. W. King, Jr., U. S. Public Health and Marine Hospital Service, Washington.

1904. Professor Kitasato, Tokio, Japan.

1903. Professor Robert Koch, Institut für Infektionskrankheiten, Berlin, Germany.

1904. Dr. W. Kolle, Institut für Infektionskrankheiten, Berlin, Germany.

1903. Professor A. Laveran, Institut Pasteur, Paris, France.

1904. Dr. Edouardo Liceaga, Mexico City, Mexico.

1903. Sir Patrick Manson, 21 Queen Anne St., Cavindish Sq., W., London, England.

1903. Dr. Charles J. Martin, Lister Institute of Preventive Medicine, Chelsea Gardens, London, England.

1904. Professor Elie Metchnikoff, Institut Pasteur, Paris, France.

1903. Dr. F. Montezambert, Director of Public Health, Ottawa, Canada.

1903. Dr. William Murrell, 17 Welbeck St., Cavendish Sq., W., London, England.

1903. Professor George H. Nuttall, Cambridge, England.

1904. Dr. Ogata, University of Tokio, Tokio, Japan.

1908. Dr. R. M. O'Reilly, Surgeon-General U. S. Army, Washington.

1905. Dr William Osler, Oxford, England.

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1903. Dr. M. J. Rosenau, Hygienic Laboratory, Washington.

1904. Dr. Ronald Ross, Liverpool School of Tropical Medicine, Liverpool, England.

1904. Professor Roux, Institut Pasteur, Paris, France.

1903. Dr. D. E. Salmon, Bureau of Animal Industry, Washington.

1904. Dr. Sanarelli, Rio de Janeiro, Brazil.

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1903. Dr. George M. Sternberg, Wills Mountain Sanitarium, Cumberland, Maryland.

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1906. Professor Henry B. Ward, University of Nebraska, Lincoln, Nebraska,

1903. Dr. William H. Welch, Johns Hopkins Hospital, Baltimore.

1908. Dr. Walter Wyman, Surgeon-General U. S. Public Health and Marine Hospital Service, Washington.

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A BRIEF CRITICAL REVIEW OF A YEAR'S PROGRESS IN TROPICAL MEDICINE.*

By James M. Anders, M. D., LL. D.,
Philadelphia,

Professor of Medicine and Clinical Medicine in the Medico-Chirurgical College; Consulting Physician to the Jewish Hospital; Consulting Physician to the Widener Home for Crippled Children, etc.

It has been an honor, highly appreciated, to serve as the presiding officer of a body so distinguished as that of the American Society of Tropical Medicine during the year just ended. Before taking up the theme of my brief discourse, I desire to convey to the officers, more particularly to the efficient secretary, Dr. Swan, whose enterprise deserves unstinted praise, my grateful acknowledgment of the singular zeal manifested in the executive work of this society. Especial commendation is also due the members for increased activity and greater fruitfulness of results in the individual study of tropical affections during the past year. The growing importance of this special field of medicine is becoming rapidly evident, and it is equally clear that a thorough and systematic investigation of this class of diseases in the immediate future is vital to the progress of medical science and art in America; and to appreciate this truth it is only essential to grasp the changed conditions—social, industrial, hygienic

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*Address of the president delivered at the Annual Meeting of the American Society of Tropical Medicine, held at Johns Hopkins University, March 28, 1908.

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—growing out of the acquisition of our new dependencies.

The present state of affairs has already called forth a practical rearrangement of the themes pursued, and labors of, governmental officials, sanitarians, clinicians, and research workers. But the present activities in the domain of tropical medicine may be regarded as being but a feeble foretaste of what the future inevitably conceals. Tropical diseases have been among the last to engage the serious attention of trained scientific investigators, although many members belonging to this extensive group have been imperfectly known and described from the remotest antiquity. Among the influences that will count for much in determining the extent and nature of this work to be carried forward in the immediate future for the better service of our science and art, the American Society of Tropical Medicine should, and doubtless will, take conspicuous rank. If I mistake not, this new society, with the light of dawn still upon it, is gripped with a high purpose, and destined to fulfil its great promise.

In devoting attention to the elucidation of the subject, the undertaking should have reference to well defined points of view—e. g., ætiological, pathological, clinical, therapeutical. In order to achieve satisfactory and permanent results, these different phases should receive separate consideration, although an intimate and practically important interconnection between them must be recognized. The earlier work should aim to obtain sure ætiological and pathological facts or evidence, for in the absence of a knowledge of the necessary causes of tropical diseases and a clue from their pathology we shall continue to remain ignorant of, or, at all events, incapable of interpreting their clinical behavior. On the other hand, systematic, uniform, and properly directed investigations cannot fail to achieve much needed information available for practical uses.

In the case of the infective diseases, at all events, the practical solution of the issues involved must come from ætiology and pathology. No large measure of professional opinion, expressed or entertained on any medical subject can receive adequate support either from clinical observation or therapeutical tests alone. Considerable thought, therefore, should be given to the order of development of the vast field of research in question, and to the thread of connection between the different aspects of the complicated subject.

This, then, is the pathway to be trodden, my learned coworkers, if we would venture to hope to bring this extensive field of investigation into that state of forwardness which characterizes our positive knowledge of many nontropical diseases. Much has hitherto been discovered and announced to the scientific world, but more is still enveloped in obscurity, to be elucidated, as intimated before, by appeals to bacteriology, parasitology, morbid anatomy, and morbid physiology, through the aid of which the clinical symptoms manifested may be rationally interpreted.

Whilst the year just ended has witnessed but few, if any, epoch making discoveries, the net gain may be said to have been considerable, and is an augury warranting the most favorable predictions for the future. It is to be recollected that the magnitude and complexity of the problems awaiting solution can scarcely be appreciated by an enlightened profession, as yet imperfectly acquainted with the manners, habits, and customs of the peoples of our newly acquired territories.

To attempt to give a complete review of the progress actually made during the previous year would lead beyond the scope of this address; I shall, therefore, be constrained to content myself with a brief chronicle of the more important advances gained during that short period of time. Mere theoretical expressions, unsupported by proof, will be rigorously omitted.

Foremost among tropical affections comes plague, and magnificent recent work has been done in relation to the ætiology, more especially the modes of conveyance of the bacillus. The recognition of the fact that the plague bacillus may be carried from one rat to another by the rat flea resulted from the labors of the British Plague Commission working in India.[1] During 1907, the previous experiments of the commission have been entirely confirmed, and additional observations, which have contributed much to systematic science, have been conducted.[2]

It was conclusively shown that rats could be infected by feeding them with the viscera of dead plague rats, and that in such cases the site of the bubo was the mesentery. *Per contra,* cervical bubo is the rule in naturally infected rats, hence it is obvious that natural intestinal infection rarely, if ever, occurs. Evidence to show that the infected fæces of the flea may carry the infection to the flea bite sustained by man has been advanced.

It was proved that the Indian rat flea (*Pulex cheopis*), under certain circumstances, will readily bite man—a fact which has long been the subject of controversy. Rothschild has pointed out that this species of flea is the commonest one found on house and port rats in many parts of the world, and that it is identical with the *Pulex pallidus* found in Australia and the *Pulex philippinensis* found in Manila—localities where plague has repeatedly appeared. The *Pulex irritans* and *Ceratophyllus fasciatus* were also shown by experiment to be capable of infecting animals in a few instances, and it is of prime importance that their exact influence in the transmission of plague from rat to man should also be determined.[3]

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[1] *Journal of Hygiene,* Cambridge Press, Extra Plague Number, September, 1906.

[2] *Journal of Hygiene,* Extra Plague Number, July, 1907.

So strongly has the entire medical profession become impressed with the truth of the view that the principal, if not the only, means of transmission has been accurately determined to be the flea, that no invincible obstacle to the serious business of the United States Public Health and Marine Hospital Service and State and municipal authorities in applying antiplague measures will, it is hoped, be permitted to exist in future. Granted that every facility be provided for the operation of these organized bodies, the impracticability of absolute prevention must, owing to the peculiar mode of transmission, appear evident. Finally, the necessity for united action with a view to exterminating rats and fleas in infected localities will be universally acknowledged.

Haffkine[4] has recently described the present position of inoculation in an important address delivered to the Epidemiological Society of London on the Present Methods of Combating Plague. His conclusions were:

1. Natives of India are more susceptible to plague than Africans, Europeans, and some other races, but the inoculation treatment reduces the liability to attack to less than one third of that in noninoculated. 2. In one third of the cases which occur in the inoculated the recovery rate is at least double that in the noninoculated, the ultimate result

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[3] Editorial, *Journal of the American Medical Association,* December 28, 1907. *Public Health Reports,* December 13, 1907.

[4] *Journal of the American Medical Association,* January 4, 1908.

being a reduction in the plague mortality by about 85 per cent. 3. All the cases of plague in inoculated Europeans have ended in recovery. 4. Inoculation is applicable to persons already infected and incubating the plague and prevents the appearance of symptoms, or else mitigates the attack. 5. In natives of India the degree of immunity conferred by inoculation, though it gradually diminishes, lasts during several outbreaks of the plague. 6. In Europeans the effect has not yet been seen to disappear since its introduction in 1897.

Reference should be made to the exhaustive studies of Richard Strong[5] in plague immunity. This observer doubts the protective value of Haffkine's prophylactic, while certain Indian physicians emphasize its great value in lessening plague incidence and plague mortality. For example, W. J. Simpson,[6] in the Croonian Lectures on plague, stated that one injection of three cubic centimetres of Haffkine's prophylactic is sufficient to protect during an existing epidemic:

> Inoculation is powerless to arrest the disease in those in whom the symptoms have already appeared or develop in a few hours after inoculation. Inoculation mitigates or aborts the disease in those who are in the incubation stage or have been infected three or four days previously.

Strong advocates the injection of attenuated living cultures of *Bacillus pestis* as a method of immunization. He found natural plague aggression effective in animal experiments, but owing to the great difficulties encountered in its preparation this will probably not be generally adopted. Strong also demonstrated the fact "that the development of the immunizing substances is quite independent of that of the agglutinins."[7] Strong arrives at the conclusion that in sera possessing immunizing power no bactericidal action can be shown to exist. He insists that inoculation against plague with suitable cultures is not infallible on account of individual variations in susceptibility to infection and in natural resistance. There is a consensus of opinion that inoculation is powerless to influence the general course of the disease after it is well characterized clinically.

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[5] *Philippine Journal of Science,* June, 1907.
[6] *Journal of Tropical Medicine and Hygiene,* August, 1907.
[7] *New York Medical Journal,* October 20, 1907.

The work of Ashburn and Craig,[8] in connection with *Filaria philippinensis,* is especially worthy of notice, and among the conclusions reached are the following: (a) That the complete development of *Filaria philippinensis,* discovered by them in 1906, has been followed in the mosquito, *Culex fatigans;* (b) that the *Filaria philippinensis* is distinguishable from other filariæ "both in the blood and during the developmental cycle within the mosquito"; (c) that as regards the time of its occurrence in the blood, this organism presents no periodicity. The same observers have, by their persistent investigations into the ætiology of dengue, thrown an important sidelight upon that subject. Of their conclusions, a few merit enumeration here:

(a) The specific cause is most probably ultramicroscopic in size, neither bacterium nor protozoon being demonstrable in either fresh or stained specimens of dengue blood by the microscope or in bouillon blood culture; (b) the disease is characterized by a well marked leucopenia, the polymorphonuclear leucocytes being decreased, as a rule, while the small lymphocytes are decidedly increased; (c) dengue can be transmitted by the mosquito, *Culex fatigans,* hence it is probably not contagious, but infectious in the same manner as is yellow fever and the malarial fevers. It should be pointed out that Schaudinn, Novy, and others suspect that both dengue and yellow fever are caused by protozoon parasites.

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[8] *New York Medical Journal,* June 15, 1907.

Musgrave[9] has observed seventeen cases of paragonimiasis, eight of which came to necropsy, in Manila, during the year 1906 and the early part of 1907; he has contributed an exhaustive study of this infection, based partly upon the post mortem findings and partly upon close clinical studies of the cases observed. The course of the disease is usually chronic, although an acute form is recognized with secondary infection, as a rule. Again, the condition may be either generalized or localized. An assured diagnosis rests solely on the finding of the ova of the trematode in the sputum, in the fæces, the scraping from ulcers, or in fluids and tissues removed at operations. Until more is known of the life history of this parasite, satisfactory prophylactic measures cannot be indicated. The subject is of distinct importance to this body, since imported cases have been met with in the United States and will probably be more commonly found in the future.

Concerning the ætiology of yellow fever, the results of recent investigations, while failing to demonstrate the presence of any organism having ætiological significance, are strongly suggestive that the disease is due to a spirochæta. In the *Public Health Reports* for May 3, 1907, Stimson describes an organism which he observed in the kidney of a yellow fever patient, following the method of Levaditi, its general appearance suggesting a spirochæta. But though specificity cannot be assigned to this organism, without ample confirmation, it is undoubted that the blood picture closely resembles that of diseases known to be caused by protozoon parasites.

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[9] *Philippine Journal of Science*, B. Medical Science, March, 1907

During August, 1907, a few cases of yellow fever were reported from Cuba, but, as was to be expected, no widespread epidemic was kindled thereby. An important lesson is taught the medical profession by these recurring outbreaks of yellow fever and other infectious diseases; it is that the final eradication of pestilential diseases is practically beyond human power. Again, such visitations indicate clearly enough the necessity for constant vigilance or the constant application of active measures calculated to serve as preventives, more particularly in the warm months or period of the year during which our territory is continually menaced.

Professional zeal, amounting to anxiety, to learn the specific cause of that interesting form of multiple neuritis, beriberi, has failed to receive an encouraging impetus within the past year; both the bacillus of Hamilton Wright and the coccus of Okata and Kokubo have been shown to bear no ætiological relation to the disease. The ætiological position of the organism discovered by Tscizuki[10] still lacks the needed experimental proof.

Hewlett and de Korte[11] have advanced a new tentative hypothesis, namely, that beriberi is the result of a protozoon infection, the invasive agent being eliminated through the urine, which conveys the contagion. In the urine of beriberi patients were found three varieties of refractive cells, believed to be degenerate cells, or protozoa. These observers also carried out investigations bearing on the pathology of beriberi. They found a disease in monkeys showing marked similarity to beriberi; the animals were anæmic, the knee jerks either exaggerated, diminished, or absent, with œdema of the face and genitalia in some cases. The urine showed hyaline casts and highly refractive cells (supposedly protozoa), but no albumin. The animals succumbed to the disease, and post mortem section revealed changes similar to those met with in the human kidneys in this disease.

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[10] *New York Medical Journal*, August 11, 1906.

[11] *Journal of Tropical Medicine and Hygiene*, October, 1907.

In the recent past numerous excellent articles concerning the ætiology and nature of beriberi have appeared in medical literature. There are not a few modern writers who contend that the disease is of dietetic origin, more particularly from the ingestion of rice and fresh fish. While the controversy as to whether beriberi is a microorganismal disease or the food theory is to be ultimately accepted, the balance of testimony would appear to be favorable to the infectious nature of the disease, although it must be owned that the specific cause still remains in doubt.

Among the advances in experimental therapeutics is to be mentioned the use of vaccine prepared from cultures of *Micrococcus melitensis* freshly isolated from the spleen during life. Bassett-Smith[12] reports two series of cases, the first series consisting of twenty-two cases, with marked improvement in fifteen, the second consisting of twenty-three patients, with marked improvement in sixteen. He restricted its use to the more chronic condition, in which there was a mild, seesaw temperature without marked hectic symptoms. Fortunately, although Malta fever is regarded as an acute infection, most cases pursue a chronic course. It is important to recollect that the addition of further quantities of artifically produced toxine to a patient in the acute phases of an infectious process is likely to act detrimentally. In view of the results thus far obtained, the method of treatment under consideration deserves more extended trial.

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[12] *Journal of Tropical Medicine and Hygiene*, May 15, 1907.

During the past year the bacteriologists have continued to bestow much attention upon the subject of the ætiology of intestinal diseases, attended with the symptom complex, known as dysentery. Ashburn and Craig,[13] in a study of tropical diseases as they occur in the Philippine Islands, report, under date of June 15, 1907, that they have examined one hundred healthy men, of which seventy-two, or seventy-two per cent., have shown *Entamœba coli* in their fæces. These men were all American soldiers serving at the division hospital, Manila, P. I., with no dystenteric symptoms since residing in the Philippines. They contend that it is possible to distinguish *Entamœba coli,* as they occur in the fæces of man, from the morphological appearance of the amœba, and cite two cases which were fully corroborated by information concerning their previous history, elicited subsequent to the bacteriological examinations.

Dr. Jesse Weston Fisher[14] has recently made a bacteriological study of normal and diarrhœal stools for the detection of organisms belonging to the dysentery group; he employed thirty-seven patients. Of these eighteen were healthy, and nineteen suffered from mild diarrhœa. The evidence, as it stands from these investigations, leaves little room for doubting that diarrhœal cases in which blood or bloody mucus are found in the stool, all show the presence of the *Bacillus dysenteriæ* of the Flexner type. Thus but two exceptions of mild grade were noted in Fisher's series; one of these showed a bacillus of the Shiga type and the other of the Duval lactose fermenting type. It is worthy of notice that the Shiga type may be the exciting cause of mild diarrhœas, but it is not found in normal stools. On the other hand, a "dystentery like organism" called *Bacillus F.* was recovered from 44.4 per cent. of normal stools, "from the stools of 10.5 per cent. of cases of simple diarrhœa, and from the stools of 0.01 per cent. of cases of dysentery." This organism was found to inhibit the growth of both the Shiga and Flexner types of bacillus dysenteriæ in test tube cultures, and in agglutination and absorption experiments the organism produced specific agglutins for itself, but not for types of dysentery, colon or typhoid.

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[13] *Loc. cit.*

[14] *Journal of Medical Research,* May, 1907.

Two cases of gangosa—a destructive ulceration and gangrenous disease of the palate and nose—have been reported within the past year, one by Stitt,[15] observed at a naval hospital at Canacoa, and the other (a fatal case) by Musgrave and Marshall,[16] occurring in a male Filipino, who had never been away from the island of Luzon. A bacteriological examination of the scrapings from the lesions proved negative in its results. Musgrave and Marshall give the details of the histological examination of the tissues; they regard the condition as distinct from syphilis, yaws, and tuberculosis, although finding themselves on difficult ground, owing to the absence of any organism having ætiological significance, a positive expression of opinion is wisely withheld.

Since the recent publication of the article by

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[15] *U. S. Naval Medical Bulletin,* July, 1907.

[16] *Philippine Journal of Science,* August, 1907.

[17] *Journal of the American Medical Association,* December 7, 1907.

Yount and Sudler[17] on the subject of human myiasis from the screw worm fly, considerable interest has been awakened in the subject. The disease is believed to be not rare, and the twenty-three cases reported by the authors occurred during a single summer. In man its results are always serious or fatal if not early and properly treated. The disease attacks many lower animals—e. g., horses, cattle, sheep, hogs, and it has been observed in many countries, islands of America, North America, Cuba, Mexico, Brazil, Venezuela, Chile, and New Holland. According to Snow, it is common from Argentine Republic to Canada. In the vast majority of cases, the site of the attack is the nasal mucosa, where it produces ulceration often associated with necrotic or gangrenous changes.

These observers point out that "a chronic rhinitis or otitis or even uncleanliness attracts the female fly, as does any exposed wound or ulcer." It is also noteworthy that sleeping in the open air gives the fly an opportunity to deposit its eggs, after which the larvæ are capable of boring into healthy as well as diseased tissue. Yount and Sudler present the symptomatology and diagnosis of the condition in the article referred to, and it is interesting to observe that chloroform employed in the form of a spray is counselled for diagnostic purposes, as it serves to bring the parasites to light, and also as the most effective measure of treatment.

Among the more important tropical and subtropical diseases stands uncinariasis, which has received a large share of professional attention, and the recent work of E. C. Shattuck,[18] of Manila, on this disease is worthy of elaborate mention. The hospital system, consisting of Bilibid Prison, with 3,800 prisoners, a hospital of 150 beds for general purposes, and a quarantine pavilion in which all recent admissions to prison are kept for a period sufficient to develop any latent infection, furnished ample opportunity and scope for systematic and satisfactory observation. All new admissions were regularly examined for intestinal parasites, and appropriate treatment instituted in infected cases.

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[18] *American Medicine,* December, 1907.

Approximately 1,000 examinations of quarantine cases have been made to date. Of 530 prisoners admitted to the hospital for treatment, there were 243 cases of uncinariasis, sixty-three of amœbic dysentery, three of balantidium coli infection, 186 of ascaris infection, seven of tænia, and the remainder acute dysentery.

There is a tangible basis for the belief that thorough, careful observations on this broad line will lead to the discovery of points of great interest and importance for practical purposes. As Shattuck pertinently remarks, however, the work on uncinariasis is hardly more than begun, although the prompt recognition of the condition, from the microscopical examinations referred to before, has doubtless already contributed materially to the marked decrease in the death rate during the past half year. Extended investigations have been carried out simultaneously in connection with the treatment, and as the result preference is given to eucalyptus rather than thymol, which was formerly the generally accepted remedy.

Authors are in agreement that prevention of uncinariasis must lie in two directions: First, personal cleanliness, and, second, the prompt disinfection of the fæces. Of less, though considerable import, is the question of the prevention of fæcal deposits in moist places and near to dwellings.

In the recent work on *Anœmia in Porto Rico,* by the Permanent Commission for the Suppression of Uncinariasis, it is estimated that ninety per cent. of the population suffers from this formidable scourge. The Commission treated 89,233 patients with the following result: Complete cure in 25.71 per cent., practical cure in 17.88 per cent., and 40 per cent. are still under treatment. Of those treated, 0.21 per cent. died. The treatment consisted in the repeated administration of thymol and betanaphthol, preceded and followed by a saline. Eucalyptol was tried, but was not found efficacious. At autopsies renal degeneration rather than inflammatory lesion was found.

An International Conference on Sleeping Sickness was held in London (June, 1907), and it is a matter of deepest regret that its deliberations and reflections can merely be touched upon in this place. Among the conclusions arrived at, based on present knowledge of the subject, is that sleeping sickness is due to the *Trypanosoma gambiense,* "propagated in main by the *Glossina palpalis,* or tsetse fly, although other species of flies, notably of the glossinæ, cannot be excluded."[19] Methods of prevention concerning both the patient and the fly were suggested and considered, and among the most noteworthy are: Police sanitation of infected individuals in order to prevent the transportation of the parasite, the avoidance of the establishment of camps or habitations in localities where the tsetse fly lives, particularly to keep clear of infected localities, attention to the borders of streams and lakes (clearing out the brush, etc.), the places inhabited by the flies, and, finally, the protection of houses, closets, etc., by mechanical means in order to keep out both glossinæ and various species of anopheles. From the therapeutic side, the conference approved the use of arsenic, which, by diminishing the number of trypanosomes in the blood, also diminishes the chances of contagion. Koch[20] has suggested that trypanosomiasis may be transmitted by sexual intercourse.

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[19] Editorial Article, *New York Medical Journal,* September 7, 1907.

The formation of the International Society of Tropical Medicine during the Fourteenth International Congress of Hygiene and Demography, which was held in Berlin in September, 1907, was an event well worthy the serious notice of this society. The objects of the society are twofold: First, to bring together the societies of tropical medicine of different countries for the purpose of an exchange of views, and, second, to hold a congress of tropical medicine once in three years.

The affairs of the international society have been in the hands of a committee of management, composed of two representatives of each national society of tropical medicine, and the authorized members on said committee from the United States are Dr. H. G. Beyer, of the Navy, and Dr. Richard P. Strong, of the Government Biological Laboratories at Manila.

Mention should also be made of the establishment of two new journals, namely, *The Annals of Tropical Medicine and Parasitology,* published by The Liverpool School of Tropical Medicine, of which the first number was issued under date of February 1, 1907, and *The United States Naval Medical Bulletin,* published in Washington, the first number appearing in April, 1907.

1605 Walnut Street.

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[20] *Journal of Tropical Medicine and Hygiene,* February 15. 1908.

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A REVIEW OF RECENT WORK ON SPIRILLAR FEVERS.*

By F. Percival Mackie, F. R. C. S. (England),
Bombay,
Captain, Indian Medical Service; Assistant to the Director, Bombay Bacteriological Laboratory; Fellow of the Royal Society of Medicine; Fellow of the Society of Tropical Medicine and Hygiene; Corresponding Member of the American Society of Tropical Medicine.

Published under the Imprimatur of the American Society of Tropical Medicine.

The association of spirilla with human disease has been recognized since the discovery by Obermeier (1) in 1873 of the organism which bears his name, but it is only during the last few years that the parasitology of this class of fevers has received particular attention.

In the light of facts which were discovered concerning African tick fever, the spirillar diseases which are met with in other parts of the world have been the subject of careful attention, and the results obtained are so important that I think it of interest to pass them in review and to consider some questions which have arisen out of our extended knowledge.

Professor Novy and others have suggested that the various relapsing fevers are caused by different spirilla, and it is partly with the object of collecting evidence on this point that this paper has been written. The question concerning the zoological rela-

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tions of the spirillum will also receive attention and reference will be made to some animal diseases due to spirilla in so far as they throw light on similar phenomena in man.

For the sake of comparison, and to make what may prove to be a purely arbitrary division of the subject, I propose to deal separately with the relapsing fevers which are met with in the four continents and the literature, so far as it is accessible to me, has been examined with that object.

The fevers and their parasites are conveniently referred to as follows: The European disease and the *Spirillum Obermeieri;* the African disease and the *Spirillum Duttoni;* the Asian disease and the *Spirillum Carteri;* and the American disease, with which we may associate the name of Professor Novy (*Spirillum Novyi*).

Pending the decision as to its zoological position the parasite is referred to as a "spirillum" rather than as a "spirochæta."

I. SPIRILLUM OBERMEIERI.

Morphology.—Length, from 12 μ to 45 μ; breadth, from 0.3 μ to 0.5 μ. The number of curves varies from four to sixteen, and they are sharp and fairly regular. The ends are pointed. No structure can be made out even under the highest powers, though Obermeier (1) described irregularities in the course of the filament which were probably due to commencing degeneration.

Koch originally described one or more flagella at either end of the spirillum, and the observation was confirmed by Karlinski (2).

Quite recently Fraenkel (3) has shown the presence of peritrichous flagella of extreme tenuity like those described by Borrel (4) in the case of *Spirillum gallinarum* and *Spirillum Duttoni.*

Provazek (5) and also Schellack (6) believe that these lateral flagella are but artefacts produced by Zettnow's flagella method.

Most observers agree on the absence of an undulating membrane, though such has been described by Schaudinn (7) and also by Leishman (8).

The movements of the spirilla are varied; there are three easily distinguishable. The first is a rapid, corkscrew motion accompanied by translation from one part of the field to another; this is seen at the beginning of an attack, when the parasite is most vigorous. The second consists of an undulatory movement of the whole thread, and is seen as the crisis approaches or when the spirilla are losing their vitality—Weigert (9) and Moczutkowsky (10). The third is a swaying motion and is the last sign of vitality. To these Munch (11) adds tetanic movements.

All observers have failed to cultivate the organism in vitro, though it is capable of surviving as long as a fortnight or more at room temperature (Gabritchewsky) (12). It lives longer in blood drawn early in the disease than at the critical period, and longer at room temperature than in the incubator or in the refrigerator.

The relation of the spirilla to human disease.—They are present in the blood stream from the onset of the fever until the crisis, when they suddenly and totally disappear. They then collect in the spleen (Metchnikoff) (13), (Soudakewich) (14). Many writers have examined the secretions and excretions, and all agree with Engel (15) and Moczutkowsky (16) that the spirillum is never found except in the blood stream. Intrauterine infection of the fœtus has been observed by Albrecht (17). There is a progressive polynuclear leucocytosis falling with or about the time of the crisis.

Transmission to laboratory animals.—Until recently all animals, except monkeys, were stated to be immune, but lately Fulleborn and Martin Meyer (18) and also Uhlenhuth and Haendel (19) have shown that, although mice cannot be infected directly from human sources, yet if the spirillum is first passed through a monkey then infection can be set up in mice. The infection does not seem to be severe, and serial passages cannot be obtained. Inoculation with apyrexial blood is negative (Bullock). Fraenkel (21) noted that some mice became infected by devouring the carcase of a mouse which had died of the disease. Uhlenhuth and Haendel (22) failed to corroborate this, but found that the mice which had so eaten had acquired some degree of immunity. The same experimenters found that monkeys suffered from a severe attack of the disease, which was followed by a relapse. Rats and mice inoculated by the peritoneal route showed a blood infection in twenty-four hours, reaching a maximum in forty-eight hours. Spirilla persisted until the third day, but were then avirulent, owing to the presence of antibodies.

The question of natural transmission.—This is believed to be due to insect agency, and suspicion has fallen particularly on the bedbug (*Cimex lectularius*). This insect has therefore come in for a large share of attention, and Tictin (23) and Karlinsky (24) assert to have transmitted relapsing fever by its agency. Their methods are open to criticism, as success was not obtained by infection through bites, but by bruising the bodies of recently fed insects in a mortar and injecting the resulting material into monkeys. They also found that bugs taken from infected dwellings frequently harbored spirilla, and, further, they were able to demonstrate them in the stomach contents of bugs as late as thirty days after feeding. Breinl and Kinghorn (25) tried to transmit both *Spirillum Obermeieri* and *Spirillum Duttoni* by bugs, but failed, and concluded that these insects would not be found capable of conveying the disease.

The question of immunity.—Immunity is conferred by an attack, but it is not very marked, nor does it last long.

Metchnikoff (26), writing in 1897, believed that the disappearance of the parasite was due to phagocytic action, which took place principally in the spleen. In support of this view Soudakewitch (27) found that splenectomized monkeys passed through a very severe attack of the disease, in which the crisis failed to appear and death often resulted.

Tictin (29) (working with *Spirillum Obermeieri*) and Lamb (28) (with *Spirillum Carteri*) failed to show any difference between normal and spleenless monkeys. Gabritchewsky (30) and Lowenthal (31) showed the existence of active spirillicidal substances in the blood, which increased up to and beyond the crisis. According to them, when these bodies have reached a certain pressure precipitation of the spirilla takes place, which marks the crisis, following which they are phagocytosed in the spleen.

Schellack (32) does not believe in the destruction of spirilla by phagocytes, but in extracellular destruction in the liver and spleen.

Many observers have demonstrated the presence of spirillicidal substances in the blood and the destructive effect of the serum of recovered animals on active spirilla. These facts have been used to distinguish the various spirillar infections from each other and from other diseases, and have formed the basis of treatment by serum therapy. Gabritschewsky (33) and Lowenthal (34) produced such a serum from horses and injected it into patients suffering from the disease. They reported that the treatment seemed to prevent the occurrence of relapses, but on the whole the results were indefinite.

The course of the disease is unaffected by drugs.

Morbid anatomy.—There are no characteristic changes in the organs of persons who have died of relapsing fever; such morbid appearances as are met with are those generally associated with severe septicæmia. Thus, there is marked fatty degeneration of the heart muscle, whilst the spleen and liver are enlarged, and show necrotic patches, which are due either to infarction or to local concentration of spirillar toxines.

Hæmorrhages are not infrequent, especially in the kidneys. Some degree of bronchitis is constant. The bone marrow shows necrotic patches, which are apparently due to infarction.

2. SPIRILLUM DUTTONI.

Morphology—Ross (35) gives the length as varying from 15 μ to 45 μ. Dutton and Todd (36) give 13 μ to 43 μ, and describe it as having pointed ends, from 2 to 6 undulations, and of uniform staining. The width is given as from 0.2 to 0.4 μ. They describe certain Y shaped forms, which suggest longitudinal division.

Koch (37) found that the spirillum is longer than the European variety. He failed to find evidence of an undulating membrane or of longitudinal division, and did not see chromatin dots in the course of the spirillum. He saw nothing to suggest a cycle of development either in the human blood or in the bodies of ticks.

Breinl, Kinghorn, and Garrett (38) state that the length of the individual spirillum is from 14 μ to 16 μ, and they describe refractile dots in the endoplasm.

The question of flagella is controversial. The earlier observers found no evidence of terminal or lateral flagella, but Zettnow (39) describes and figures diffuse peritrichous flagella corresponding closely to those described by Borrel (40) in *Spirillum gallinarum.*

Breinl, Kinghorn, and Garrett, and later Stephens (41), deny the presence of either undulating membrane or flagella. The last named observer describes, however, a terminal whip at one end and a sheath, adding that he has seen eviscerated forms which have left the sheath still retaining its original undulations.

Commenting on this appearance Breinl and his coworkers advance similar arguments used by me in reference to Novy's spirillum, namely, that the so called flagellum is merely part of the empty and extenuated sheath.

Dutton and Todd (42) have recently published some new observations on the morphology of *Spirillum Duttoni.* The organism, they say, is ribbon shaped and consists of a central core and a periplastic sheath. The latter is continued to form a flagellumlike process and there are no peritrichial flagella. The core is composed of a series of granules interrupted by lightly staining areas. Median or terminal knot like swellings are frequent, and some thickened individuals suggest longitudinal division. Occasionally they are met with inside both red and white corpuscles, especially just before the crisis. They describe an undulating membrane, also longitudinal division, as not infrequent, and think that conjugation takes place. They also describe a change which the spirillum undergoes in the tissues, which results in a body distinguishable with difficulty from a blood platelet, and they believe it to be a sporocyst.

In the bodies of ticks they find that the spirillum undergoes a sort of encystment, which appears as "a faint blue or red spherical matrix about 5 μ to 7 μ in diameter, in which are imbedded perhaps a score of deep red granules." They believe that these sporocysts may rupture and the granules develop each into a new spirochæta.

Schellack (43) gives the maximum length of the individual as 24 μ, with 8 to 12 undulations, and the width as 0.45 μ. He has not satisfied himself as to the presence of an undulating membrane and believes the peritrichial flagella to be artefacts.

The relation of the spirillum to human disease.—All writers are unanimous in stating that the spirillum is much less common in the human blood than is the case in other spirillar infections.

Ross (44) goes so far as to say that they may not be found in the first attack, but only in the relapse.

Moffat (45) says they are sometimes "excessively scarce after the first attack."

Spirilla have not been found, except in the blood stream. There is a leucocytosis, as in the European disease.

Transmission to animals.—Ross and Milne (46), and again Dutton and Todd (47), found that certain monkeys (cercopithecus, cynocephalus) were susceptible, but that ordinary laboratory animals were not so.

Breinl, Kinghorn, and Garrett (48), however, found that most ordinary animals were susceptible in varying degrees. Thus white rats were the most so, and to a lesser degree dogs, horses, goats, sheep, rabbits, guinea pigs, rats, and mice, whilst cats, chickens, pigeons, and goldfish were insusceptible. The incubation stage in monkeys (by tick transmission) is five to seven days; each febrile attack lasts three to four days; the animals suffer from three or four relapses at intervals of from five to nineteen days, so that the whole course of the disease in these animals lasts from three to eight weeks (Todd and Dutton). The spirilla are more numerous than in man.

The monkeys only occasionally die, but small animals frequently do.

In rats the incubation stage is only a few hours, and the duration from one to forty-five days, punctuated by successive relapses. The parasites are very numerous and the mortality high. The virus is exalted by frequent passage.

The infection is capable of passing through a Berkfeld filter fine enough to keep back *Bacillus prodigiosus.* The passage of the spirillum from mother to fœtus, already described in Europe by Albrecht (49) and Spitz (50), has been substantiated by Breinl and Kinghorn (51), working with rats and the African infection.

They draw the following important conclusions:

"(1) *Spirillum Duttoni* passes through the placenta from the maternal to the fœtal circulation; (2) the majority of fœtuses carried by infected mothers are themselves infected; (3) spirilla are more scanty in the fœtal blood than in the maternal blood, but the placental and maternal blood are equally infected with the parasites; (4) the parasites in fœtal blood show no morphological change; (5) there is no tendency to abort, but few of the young animals reach maturity; (6) the young born of infected mothers possess no marked immunity either to direct inoculation or to the bite of the tick."

Natural transmission.—Transmission by ticks occurs in one of two ways: Either by direct infection from the bite of a tick which has itself previously bitten an infected person, or by the bites of ticks born of infected females.

Koch (52) showed that when a tick had taken in infected blood the spirilla disappeared from its stomach after a few days and were then to be found on the surface of the ovary, where they underwent multiplication. A considerable proportion of the ova of such a tick were infected. There was no cycle of development in the tick, and the route of the infection was not clear, for spirilla were not formed in the salivary glands.

Koch found that from five to fifteen per cent. (once fifty per cent.) of the ticks taken from infected huts contained spirilla.

Markham Carter (53) found that six out of thirty-two eggs laid by infected ticks contained spirilla. He speaks of some spirilla in the eggs as undergoing longitudinal division and refers to minor alteration in form. Breinl and Kinghorn tried to transmit the disease by the agency of bed-bugs, but failed.

Morbid anatomy.—This has been carefully studied by Levaditi and Manouelian (54) by aid of the silver impregnation process described by the former, and they come to the following conclusion: The spirilla cultivate themselves exclusively in the blood stream, and under no circumstances invade the cellular protoplasm.[1] There is no evidence of any intracellular stage in the evolution of the parasite. The spirillum, they say, causes necrotic foci in the liver, and these foci are visible to the naked eye as soft, yellow patches, and microscopically as areas of cell necrosis. These they believe to be chiefly embolic in origin and only partly due to the action of soluble toxines. They believe that the critical destruction of spirilla is essentially a phagocytic phenomenon, and does not depend at all on the direct intervention of spirillicidal substances. They find that the parasites often occupy the macrophages in curved and ringed shapes, and they consider this to indicate degeneration and not to be resting forms, as Schaudinn and Prowazak believed. Similar curved spirilla are seen coiled around the red blood cells, though these cells are never penetrated. Sawtchanks (55) demonstrated that fixative substances (opsonins) acted on the spirilla of recurrent fever, rendering their phagocytosis more easy.

Levaditi and Roche (56) estimated the influence of opsonins on the mechanism of the crisis and came to the conclusion that the destruction of spirilla at this period was not due either to bacteriolysins or to opsonins, and that the latter only came after the disappearance of the spirilla from the blood stream.

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[1] Herein this spirillum differs from the *Spirillum gallinarum* and from *Treponema pallidum*, which are both true tissue invaders. Bertarelli has described *Spirillum Obermeieri* as being present in the interior of splenic cells, but the French observers named look upon them as an agonal invasion.

3. SPIRILLUM NOVYI.

Morphology.—Our knowledge of this spirillum is due partly to the investigations of Norris, Pappenheimer, and Flournoy (57), but particularly to those of Novy and Knapp (58). These observers give the length of the smallest spirillum as from 7 to 9 μ and of the longer forms as multiples of those numbers, indicating end to end union. There are but two or three turns to the short forms, and the curves are sharp and regular. The American spirillum is shorter and finer than either the African or European. A well marked terminal flagellum is pictured, and the writers say there are no lateral ones. Fraenkel (59) and others, however, working with Novy's spirillum in Europe, differ and find the disposition of the flagella as being identical to that in the other two, that is, peritrichous.

The mechanism of movement is similar to that of the other spirilla described, and division is said to be always transverse and never longitudinal. Norris and his coworkers describe the cultivation of the spirillum in citrated blood, but Novy and Knapp, following their methods, failed to convince themselves that true multiplication took place. The latter experimenters have since (60) by following the method adopted by Levaditi (61), who worked with *Spirillum gallinarum, Spirillum Duttoni,* and *Spirillum refringens,* succeeded in cultivating the American spirillum in collodion sacs placed in the peritoneal cavities of white rats. The spirilla multiply exceedingly under these conditions, and have been carried through twenty generations. The authors conclude that neither red nor white corpuscles are necessary to the multiplication of the spirilla, and that there cannot therefore be an intracellular stage.

Transmission to animals.—Monkeys, white mice, and tame and wild rats were found susceptible to the American spirillum, and with the exception of the last named all are subject to relapses. White mice are especially susceptible, and show an infection within twenty-four hours of injection, which persists up to the end of the third day. The infection is very heavy.

The mechanism of immunity.—Novy and Knapp (62) have paid special attention to this part of the subject, and their results are thus summarized: "A powerful specific germicidal body is present in decline and in recovered blood, notably in blood of hyperimmunized rats. This body does not originate after the blood is drawn, but exists within the living animal. An immunizing body is also present, and is probably distinct from the germicidal agent."

Pfeiffer's phenomenon can be demonstrated in vitro and in vivo. In the peritoneal cavity of hyperimmunized rats the spirilla are killed almost instantly, after which they are taken up by the macrophages or large mononuclear cells. Active immunity follows recovery from the infection. By successive injections of spirillar blood this immunity can be increased to a remarkable degree.

Passive immunity can be imparted by injections of recovered or hyperimmunized blood. Both active and passive immunity may last for months.

Hereditary immunity can be obtained, and is probably the result of infection in utero.

Preventive inoculations can be successfully made in rats, mice, and monkeys. Infected rats, mice, and monkeys can be promptly cured by injection of hyperimmunized blood. Subsequent relapses, if any, can be prevented by curative doses of blood.

Agglutination of spirilla occurs in vitro and in vivo under the influence of recovered or hyperimmunized blood. To a slight extent it occurs during crisis. The agglutination, germicidal, and immunizing properties of recovered blood can be used in the serodiagnosis of relapsing fever, and also for the identification of spirilla. The evidence points to the existence of a group of relapsing fevers.

It is not clear whether relapsing fever is indigenous to the American continent, or whether it was originally imported. It appears to be very rare, and clinical descriptions of the disease are not accessible to me.

I am not aware of any theories as to its transmission among human beings.

An outbreak of relapsing fever has recently been described by Franco, of Bogota, in Columbia, South America, and reported by Blanchard (63). The spirillum resembled that of tick fever, and was associated with the bites of ticks, and of these Blanchard incriminated particularly *Ornithodorous turicata.*

4. SPIRILLUM CARTERI AND ASIAN RELAPSING FEVER.

Morphology.—Length, 12 μ to 16 μ, by 0.3 to 0.5 μ wide. These are the measurements of the common form seen in circulating blood, which show no sign of dividing. Shorter individuals measuring 7 to 8 μ are sometimes seen. In the organs of infected lice spirilla only 2 or 3 μ long are seen; these are in the form of a single S curve, and would be irrecognizable were it not for their association with those of normal dimensions.

Novy has noticed the presence of similar short forms in the substance of phagocytes, and it may be that these represent the essential units of which spirilla are composed.

These short individuals show no fragmentation or other sign of degeneration. In the healthy spirillum no structure has been made out, but when degeneration commences the cytoplasm breaks up into minute dotlike segments, which give the chromatin reaction, but are not acid fast.

There is a terminal filament at one or both ends, similar to those described and figured by Novy as flagella. I have hitherto looked upon these as empty sheaths for reasons already advanced (64).

Multiplication takes place in the circulating blood by transverse division, but recently I have seen appearances in the stomach of the louse which strongly suggest conjugation or longitudinal division.

I have not been able to demonstrate an undulating membrane. Cultivation has not yielded positive results, but multiplication takes place in centrifugalized citrated blood for the first twenty-four hours and then stops.

The spirillum has been recovered alive from blood three weeks after withdrawal from the body.

The relation of the spirillum to human disease.—The spirillum is readily found in the blood during the acute attack, becoming more frequent as the crisis approaches, at which time it completely disappears.

The secretions and excretions have since Vandyke Carter's time been held to be free from infection, and some experiments recently performed by me bear out this statement. It is true that several times spirilla of some sort were present in the urine, but inoculation of them into monkeys failed to produce the disease. The spirillum, moreover, is present in the menses, in placental blood, and in the blood from hæmorrhages. A series of cases among the staff of a lying-in hospital in Bombay appeared to be due to infection from placental blood.

The apyrexial blood of patients has hitherto been looked upon as incapable of producing the disease, but there is some evidence which throws doubt on that observation. One carefully conducted experiment of mine showed that the spirilla appeared simultaneously in the blood of an inoculated monkey and in the relapse blood of the patient from whom it was taken. The incubation period in the monkey was delayed from the usual three days to five days. Blood taken at the same time from the human patient, citrated and preserved in vitro, did not show spirilla.

In this connection it may be noted that Albrecht (65) in 1881 showed that blood drawn from patients, either one, two, or three days before a relapse was due, showed a development of spirilla even in vitro, and that the development coincided with the time of the relapse in the patient.

Dr. Row, of Bombay, has informed me of a similar observation on his part.

Carter explained Albrecht's observation by saying that spirilla appear in the blood before the temperature begins to rise, but are scarce and difficult to find, and hence, although Albrecht assumed them to be absent, they were really present, but in such small numbers as to be overlooked.

Transmission to animals.—Carter and subsequent observers failed to produce the disease in any animals except monkeys, but recently I have shown that white mice, white rats, white rabbits, black rats (*Mus rattus*), brown rats (*Mus decumanus*), and to a lesser extent guinea pigs, are all susceptible, but dogs, cats, goats, and pigeons are refractory.

The infection in animals other than monkeys is transient, and is not accompanied by marked symptoms, and the blood infection is light.

It is possible to infect monkeys by using much smaller doses of infected blood than that usually employed, and also by light scarification of the skin and application of infected blood. Further, by the use of a grooved needle, to imitate the proboscis of an insect, the infection was carried from an infected to a noninfected monkey by transpuncture. Again, I showed that monkeys readily became infected by feeding with spirillar blood; the incubation stage is prolonged from three to five days, but a typical attack follows.

These experiments show that the agency of insects would probably suffice for transmission, and, further, that such transference is probably mechanical, or, at any rate, does not necessitate the occurrence of any intermediate stage of development.

The question of natural transmission.—Ten carefully organized experiments have been made, at intervals spreading over a year, to transmit the disease from an infected to a noninfected monkey through the agency of bugs. The first experiment was successful, but the nine following ones failed.

No cases of natural transmission have taken place in the monkey room, and no monkey has ever shown natural or unexplained immunity.

The organs of bugs (*Cimex rotundatus*) have been examined with minuteness at different stages after an infected feed, and spirilla have been found with regularity up to the sixth day after feeding, but only in the stomach and only in the presence of fresh blood and without sign of multiplication. More definite results have been obtained with the body louse (*Pediculus corporis*), and the observations on the Nasik epidemic have just been published (66).

Thus fourteen per cent. of lice taken from the heavily infected boys' ward, two per cent. taken from the scantily infected girls' ward, and thirteen per cent. of artificially fed lice showed multiplication of spirilla in the internal organs. The principal seat of multiplication was the stomach of the louse and the upper part of the alimentary tract and the ovaries, and sometimes the Malpighian tubes were secondarily infected. A fluid rich in active spirilla could be obtained by gentle pressure on the heads of infected lice.

The question of immunity.—By injecting the blood of man and monkeys into monkeys and into goats a marked, though not high, degree of immunity was called out. The serum so obtained was found to have the power of killing the spirilla and producing lysis in a short time (fifteen seconds) in dilution of 1 in 20.

About 30 c.c. of such serum was injected into a patient during the height of the disease. The result was indefinite.

The observations I have made incline me to believe that the action of spirillicidal substances determines the crisis, and that phagocytosis, if it takes place at all, is carried on in the internal organs, and is of secondary importance.

I have never seen phagocytosis taking place in the blood stream, although I have frequently observed dead spirilla engulfed by leucocytes when both were kept in vitro.

Lamb found that the spleen was not of such importance in the crisis as Soudakewitch and others had supposed, for he found that spleenless monkeys did not suffer to a greater degree than normal ones. He also carried out experiments to determine the relative importance of phagocytosis and of spirillicidal substances in the mechanism of the crisis. He came to the conclusion that it was the increase of spirillicidal substances which determined the crisis, and that phagocytosis was only secondary. He advanced a theory to explain the recurrence of infection similar to that put forward by Wright and others to explain relapses in enteric fever.

According to this idea, spirilla escape by finding areas protected from the full spirillicidal pressure of the blood and remain there until such pressure has been reduced by excretion or by the production of antispirillicidal bodies. They then are able to recultivate themselves in the blood stream and so produce a relapse.

Morbid anatomy.—The very careful description of post mortem examinations in Vandyke Carter's monograph (68) serves only to leave the impression that there are no lesions characteristic of the disease. If the tissues are stained by those methods which are usually chosen for revealing bacteria or protozoa, the spirilla are demonstrated with difficulty. They are seen to occupy the bloodvessels and the tissues in the neighborhood of hæmorrhages. From this I believed (69) that the spirillum was a true blood parasite and lived only in the circulating blood. More recently by using Levaditi's silver impregnation method this view has been modified. The spirilla were seen to be scattered throughout the liver, and not confined to the bloodvessels, though it is true no special relation to the tissue cells could be demonstrated.

This observation requires substantiation, but if it is true it tends to bring *Spirillum Carteri* more into comparison with *Spirillum gallinarum* and *Treponema pallidum* than with *Spirillum Duttoni,* which, as has been shown above (Levaditi and Manouelian) (70), is a true blood parasite.

The course of the relapsing fever in man.—For the account of the European disease I refer the reader to the article Relapsing Fever in Clifford Allbutt's *System of Medicine,* i, 1905.

The African tick fever has been well described by Moffat, of Uganda, and the clinical course of the Asian disease has been most fully dealt with by Vandyke Carter. I have not been able to see any clinical descriptions of the American disease, and it is not clear how far the accounts in the American textbooks of medicine are the result of the experience of the writers and how much is taken from the classical description of the European disease.

Having studied the account of the disease from these various sources, I am in a position to call attention to certain points of difference between them.

In Europe the incubation stage varies from five to seven days, and there are generally one and sometimes two relapses. Jaundice of a mild degree is almost invariable, but bears no special relation to fatality. Pregnant women nearly always abort. The mortality varies between four to eighteen per cent., but Rabagliali (71) averages it at not more than five per cent.

The African tick fever is more severe. Moffat (72) believes there is more than one type of the disease in Africa, and contrasts that met with on the Zambesi with that with which he is acquainted in Uganda. The incubation stage is said to be only of a few hours' duration in the former, while in Uganda it is between seven and ten days. Ross and

Milne (73) in their original paper give the incubation period as being from one to five days, but Ross in Clifford Allbutt's *System of Medicine* (ii, part II, 1907) gives it as three to eight days.

The duration of the initial attack is from three to four days, and the first apyrexial period lasts five to eight days (Moffat), one to three weeks (Ross).

The number of relapses is from three to five, and if less Moffat suspects some degree of immunity. There may be as many as eleven relapses.

The disease is very much more severe in the European than in the native, in whom a partial degree of protection may be suspected.

There is a form of pneumonia, disappearing with the crisis, and in which the sputum is loaded with spirilla. Moffat also lays stress on certain eye symptoms which he looks upon as pathognomonic.

No figures as to mortality are given, though in one batch of coolies on the Zambesi the mortality is given as fifty per cent. The Uganda disease is certainly less severe.

Fraenkel (74) has compared the spirilla met with by Koch in British East Africa with that described by Dutton and Todd in the Congo district. He finds no differences in their morphology or in their action on animals, but immunity against each is powerless to prevent an attack by the other. He concludes that these two spirilla are distinct, and suggests similar relationship between them to those uniting the paratyphoid and the typhoid bacilli.

THE RELAPSING FEVER OF INDIA.

The incubation stage and the first pyrexial period and the first apyrexial interval are each of seven days' duration. Low delirium often appears after the crisis, and disappears at the beginning of the succeeding relapse. One relapse is the rule; next most commonly there is no relapse; more rarely two relapses. Choksy, who has seen 6,000 cases in Bombay in recent years, has only once noted five relapses.

True pneumonia is rare, and I have never seen spirilla in the sputum. Parotitis occurs in ten per cent. of cases. Eye symptoms are rare, and are not of the type described by Moffat.

When the patient is pregnant, *abortion is the rule.*

There is a distinct type of spirillar fever called by Carter "the bilious typhus type." It is associated with great enlargement and tenderness of the liver and spleen, with much tympanites and marked jaundice, the presence of muttering delirium, and the absence of a crisis.

The mortality is very high. McCowen (75) had a series of seventy-nine cases in a native regiment. The total mortality was 20.25 per cent., but whereas sixty-one cases of the ordinary type gave a mortality of 6.5 per cent., there was a mortality of 66.6 per cent. among the eighteen cases of the bilious typhus type. Vandyke Carter gives the mortality of all cases as 18.02, but Choksy finds it varying from fifteen per cent. in 1897 to forty-three per cent. in 1901, and averaging thirty-eight per cent. during the last seven years.

The mortality among children in Bombay during that time was only eleven per cent.

It is possible that plague may have influenced the relapsing fever rate in Bombay.

A COMPARISON OF HUMAN SPIRILLA.

Morphology.—The American spirillum is described as being shorter than the other three. Uhlenhuth and Haendel, comparing the European, African and American spirilla, found that the African was the most vigorous and was less typically spiral in shape and formed more open flexures. The American showed the most regular and typical spirals, and was less vigorous, while the European was intermediate. Schellak (77) took great precautions to make accurate comparisons, and found that the flexibility and the intensity of movement of the European was less than the Russian, but greater than the American.

He finds that there is a difference in size; thus the maximum length without sign of division of the African is 24 μ and width 0.45 μ; maximum length without sign of division of the American is 17—20 μ and width 0.31 μ; maximum length without sign of division of the European is 19—20 μ and width 0.39 μ.

I was able to compare the American spirillum with the Asian, and I found a markedly different picture, and have no hesitation in saying that the two could be readily distinguished by any one who was familiar with either. The American is shorter than the Bombay spirillum, and the individuals are discrete, instead of forming end to end aggregations, as the latter frequently do. It is also thinner and more delicate, and does not stain so intensely as *Spirillum Carteri.* The American is typically spiral, the Asian is rarely so. The *Spirillum Novyi* lie separately, whereas the others generally lie knotted together in twos or threes. Transverse division is more clearly marked than in the Asian parasite.

Then as regards cilial disposition. Fraenkel finds the European and the American spirilla possessed of peritrichous flagella. Novy and Knapp described only a terminal flagellum on their spirillum. Zettnow (78) found that *Spirillum Duttoni* had peritrichous flagella, but the Liverpool workers deny this, and describe a terminal whip.

I found that the Indian spirillum possessed a terminal filament which did not agree with my conception of a true flagellum. Schellak described lateral polyflagella on all three occidental spirilla, but believes them to be artefacts, splitting of the periplast, due to the various manipulations used in Zettnow's flagellum method.

Leishman (79) has examined the African, European, and Indian spirilla, but doubts whether any distinction could be drawn between them on morphological grounds. He failed to find flagella on any of them, and believes that questions of vitality, etc., suffice to explain the alleged differences of shape and so forth.

All observers are agreed that the *Spirillum Duttoni* is very scarce in the blood of human beings, and this contrasts markedly with the heavy infection met with in the case of the European and Asian diseases. Otherwise the relation of the spirilla to the human disease is similar in all.

Transmission to laboratory animals.—Here again there are noteworthy differences.

Spirillum Obermeieri is only transmissible to the smaller laboratory animals after preliminary passage through monkeys, whereas *Spirillum Duttoni, Novyi,* and *Carteri* are readily transmissible to a variety of animals. Fraenkel found that the African was more toxic than the American spirillum. Monkeys suffered as many as three and four relapses. Rats and hamsters showed one relapse, and most mice and squirrels inoculated died during the primary attack. The American spirillum does not produce a relapse in monkeys or small rodents, and the latter rarely die from the disease. Uhlenhuth and Haendel found that *Spirillum Obermeieri* produced a severe attack in monkeys, which was followed by one relapse. *Spirillum Carteri* is very mild in its effects on animals, only monkeys show any clinical manifestations, and I have never seen one (out of about eighty inoculated) die from the fever. Lamb's (80) experience was similar to mine. The other susceptible animals show no sign of disease, except the presence of spirilla in the blood.

The comparison of the clinical course of the disease met with in the four continents brings to light some marked differences.

The much greater severity of tick fever, followed as it is by four or five relapses, and the frequency of certain eye symptoms detailed by Moffat, contrast with the relative mildness of the European disease and its low mortality. The Asian type is different in showing a fewer number of relapses and by the occurrence of a very fatal type associated with jaundice and the absence of a crisis. The large mortality of relapsing fever in Bombay contrasts with that met with in selected communities in other parts of India, such as Regiments, Asylums, and Jails, and may be due to high incidence of plague in that city.

The best reason, however, for considering the spirilla to be different varieties is that afforded by the serum reaction. Fraenkel, Uhlenhuth and Haendel, Manteufel, Breinl, Kinghorn, and others have shown that animals which are completely immunized against one spirillum are still susceptible to either of the other two. Again, spirillicidal sub-

TABLE OF COMPARISONS.

	Sp. Obermeieri, European.	*Sp. Duttoni,* African.	*Sp. Novyi,* American.	*Sp. Carteri,* Asian.
Minimal length:	12 μ.	13 μ.	7·9 9 μ.	12 μ.
Shape:	Spiral,	open flexures,	regularly spiral,	open flexures.
Flagella:	Peritrichous,	peritrichous?	terminal, (Novy) peritrichous (Fraenkel),	?
Animals susceptible:	Small rodents only after passage through monkeys,	small rodents and many animals, very susceptible,	small rodents, very susceptible,	small rodents infected with difficulty.
Course in animals:	Mild,	very severe,	severe,	very mild.
Course in man:	One, sometimes two, relapses,	severe, four or five relapses,	?	severe, one or two relapses.
Parasite in human blood:	Heavy infection,	very sparse,	?	variable.
Natural transmission:	?	by ticks,	?	by lice (?)
Serum reactions:	Immune, serum without effect on *Novyi* or *Duttoni*,	immune, serum without effect on *Novyi* or *Obermeieri*,	immune, serum without effect on *Obermeieri*, *Duttoni* or *Carteri*.	immune, serum without effect on *Novyi*.

stances formed during the course of the disease only act on their own parasites and Pfeiffer's phenomenon is similarly specific.

I found by testing *Spirillum Carteri* with serum of animals highly immunized against *Spirillum Novyi* that they were quite unaffected by it, although they were quickly killed by the serum of animals which had recovered from the Indian disease.

From these data I think we may conclude that the four organisms, although closely related, are not identical, but are different varieties.

The appended table summarizes the points of divergence.

The following precis of the chief spirillar diseases of animals is appended; it is interesting as showing the morphological similarity of the various spirilla, and so emphasises the fact that such similarity is no criterion of identity, for it is certain that these animal spirilloses are clinically very different from one another and from those affecting man.

Spirillosis of fowls (*Spirillum gallinarum*).—Marchoux and Salimbeni (81) described this disease, and showed that it could be transmitted by feeding fowls with blood or excrement of infected fowls or by inoculation with infected blood. They found it was transmitted in nature by a species of tick.

The spirillum loses its virulence in blood or in the juice of the organ after forty-eight hours.

The serum of fowls which have recovered shows some immunizing properties, and the same serum in vitro possesses marked agglutinative and immobilizing action on healthy spirilla.

Writing later on the same subject Levaditi and

Manonelia (82) find that the septicæmia is not exclusively due to intravascular growth, but the spirilla invade the various glandular tissues and enter into intimate contact with the cellular elements. The crisis, which terminates the infection, is due to phagocytosis of the spirilla by the macrophages of the spleen and liver. The spirillum is capable of infecting the egg of the fowl.

Levaditi (83) in a further paper describes the development of embryos from infected eggs, and shows that death and maceration of the embryo often follows. He describes the various tissue changes associated with the disease and compares it with the course of infection in hereditary syphilis, which it resembles. As in syphilis, so in fowl spirillosis, the gland most heavily infected is the liver, which filters off the spirilla from the infected mother as the blood passes through the umbilical circulation.

A similar fowl spirillosis has been described from Egypt by Balfour (84), and lately by Reaney (85) from Central India. In both these cases the description given followed closely those given by the previous writers, and ticks were held responsible for transmission, as in the originally described disease; it is probable, therefore, that *Spirillum gallinarium* is a widespread parasite.

Spirillosis of bats.—This spirillosis was carefully described by Nicolle and Comte (86) from Tunis.

The spirillum had a length of 12 μ. to 18 μ. by 0.25 μ. width. It had pointed ends, and multiplied by transverse division. There was no evidence of undulating membrane or of any internal structure, and its movements were vibratory, contractile, and resulted in displacement.

It was transmissible to healthy bats by inoculation, and the virulence was unaltered by frequent passage. If large doses were given infection was noted in forty-eight hours; if in small doses the appearance was delayed for three, four or five days. Recovery was the rule, but relapses occurred, and later some immunity was established.

Theiler (87), describing spirillosis of cattle in South Africa, was able to transmit the disease from ox to ox and from them to sheep. The disease was specifically distinct from piroplasmosis of cattle. It was transmitted by ticks, the offspring of infected females.

Dodd (88), reviewing the subject of spirillar diseases of horses, oxen, and sheep, concludes that they are caused by identical organisms. Heanley (89) describes an epidemic of spirillar disease amongst Chinese buffalos; the disease was clinically like Rinderpest or hæmorrhagic septicæmia. The spirilla were from 16 μ to 32 μ long, and were possessed of 8 to 12 spirals; they were present as blood parasites.

Stordy (90), in the same journal, describes the disease in the horse as one of rapid course, followed by extreme emaciation. Spirilla abounded in the blood stream. He was unable to transmit it to a dog.

Many other descriptions of spirillar disease in animals might be referred to, but those given here will suffice to show how widespread these diseases are, and how similar the parasites are in their main morphological characters to one another and to those affecting man.

THE NATURE OF THE PARASITE.

The spirilla were until recently unhesitatingly placed amongst the bacteria, but in 1904 Schaudinn threw the great weight of his authority against this view. He came to this conclusion as a result of his work (91) on *Spirillum Ziemanni* and the alternation of its generations in the owl and in the mosquito, and he gave his opinion that the spirochætæ represented the flagellate stage of a sporozoon. He further stated that *Spirillum Obermeieri* and others were possessed of an undulating membrane, a nucleus, blepharoplast, and flagellum; that is, they were practically identical with trypanosomes. His deductions concerning *Spirillum Ziemanni* were found later to be of doubtful nature, and latterly he acknowledged that it was very far removed morphologically from the typical spirochætæ.

Since then the trend of opinion, led by Novy, has veered back, and many writers now consider that these organisms are more closely related to the bacteria than to the protozoa.

Novy and Knapp (92) have accumulated considerable evidence in favor of this view and they lay emphasis on the following points: Spirilla are like the bacteria in that they are structureless, possess multiple flagella, and divide transversely. On the other hand they possess neither nucleus, blepharoplast, nor undulating membrane, as the trypanosomes do. They multiply rapidly in the blood stream, giving rise to a disease which runs a short and severe course, such as is common enough amongst the bacteria, but unusual amongst protozoa.

Trypanosomes are very susceptible to plasmolytic changes, but spirilla, like the bacteria, are very little affected by changes in the osmotic tension of the fluid in which they are suspended.

Spirilla are again, like bacteria, much more resistent to heat than trypanosomes.

The spirilla retain their form under various conditions, when trypanosomes become degenerated or involuted.

Active immunity is readily called out by infections due to bacteria and spirilla, but only slowly and with great difficulty by trypanosome infection.

They also add that aerotropism is a marked feature of trypanosomes, but is absent in the case of spirilla and bacteria.

An argument upholding this view and one which I have not seen brought forward is that afforded by the leucocyte reaction. Speaking generally, bacteria, when they affect the leucocyte wave, do so by producing a polynuclear leucocytosis, whilst protozoa generally produce a leucopenia, with a relative increase of large mononuclear leucocytes (malaria, kala-azar, etc.).

Relapsing fevers are characterized by a heavy polynuclear leucocytosis, like the bacterial diseases, and I consider this as a very strong argument in favor of the bacterial affinities of the spirilla.

Some writers persist in the belief that sometimes longitudinal division and even that conjugation takes place, and some recent observations of mine in the case of infected lice lead me to incline towards this view.

Again, the methods of natural transmission by ticks and perhaps by lice is suggestive rather of a protozoon than a bacterium, but this argument is not so powerful as at first sight appears. Firstly, because no intermediate stage or involution form has yet been found in the body of the insect host, and, secondly, because insect transmission is not peculiar to protozoal diseases, for the Indian Plague Commission has recently shown (93) that plague can be disseminated by the agency of fleas.

Whilst most writers agree that spirilla differ in their characters from both bacteria and protozoa, there is considerable difference of opinion into which group they should be admitted. Zettnow (94), looking to their cilial disposition, their transverse division, and the absence of an undulating membrane, thinks they approach the bacteria, whilst Prowazek (95), who has observed their penetration into red blood corpuscles, and also on account of their reaction to solutions of sodium chloride and other weak alkalies, upholds their protozoal nature. Both are in favor of establishing a new genus for these parasites. Again, Neufeld and Prowazek (96) incline to the protozoal view because of the behavior of the spirilla to solutions of saponin and of bile salts. Bacteria, they say, are not at all affected by saponin and only the pneumococcus is sensitive to bile salts. Animal cells, however, the protozoa, and with them the spirochætæ, are readily destroyed by those agents.

A very important paper, by Swellengrebel, on the morphology of this group of organisms, has recently appeared (97), but his observations, which are in great detail, can scarcely be adequately dealt with in the limits of this paper. He studied and compared a typical spirillum (*Spirillum giganteum*) (Migula), and two spirochætæ (*Spirochæta Balbiani* Laveran and Mesnil, and *Spirochæta buccalis*).

A few of his most important conclusions are here summarized. All these organisms are possessed of a cell membrane which contains within it a protoplastic structure containing vacuoles, and these latter constitute an osmotic system like that described by Fischer (98) in the true bacteria.

The cell body of spirochætæ and spirilla is elongated, with rounded extremities, the pointed appearance at each end is due to the presence of a periplastic cap (*la calotte*). The nucleus of *Spirillum giganteum* and of *Spirochæta Balbiani* is shaped like a spiral filament and is composed of chromatin and divides longitudinally.

The division of the cell as a whole is transverse.

Division of *Spirillum giganteum* and *Spirochæta buccalis* is brought about by a nipping in, and results in the formation of a fine filament connecting the two daughter cells.

In *Spirochæta Balbiani* division is effected by transverse cleavage. At one or both ends of the organism the cells' membrane is prolonged to form *la calotte.* This process is pointed, and terminates in a fine filament—the flagellum.

Sometimes there is a tuft of cilia (*Spirillum giganteum*).

The flagella of spirilla and spirochætæ are homologous, and both arise from a chromatin granule. *Spirochæta Balbiani* has no flagellum, but the chromatin band takes origin from a granule embedded in the periplastic appendage. This periplastic appendage is an alveolar structure which winds around the cell and resembles somewhat an undulating membrane.

Spirochæta buccalis and *Spirochæta Balbiani* and *Bacillus maximus buccalis* react similarly to solutions of alkalies and acids and degenerate in the same manner.

In conclusion, Swellengrabel sees no valid reason for removing the spirochætæ from the family of Spirillaceæ (Migula), but thinks the family should be widened to admit them.

He divides the spirillaceæ into two families, (a) the flexile spirilla, (b) the nonflexile spirilla. The latter group contains the true spirilla, which may be subdivided according to the number and disposition of their flagella.

Those with a single flagellum form the genus vibrio, and those with many the genus spirillum.

Here is his scheme in full:

SPIRILLACEÆ (MIGULA).

Cells with rounded extremities forming a part of a spiral. Cell division is transverse, and is generally brought about by transverse cleavage, previous to which the cell increases in length. Sometimes division is accompanied by nipping in of the mother cell. After division the daughter cells remain for some time united by an unbroken filament. The flagella, when present, take their origin from a periplastic sheath cap, and are themselves prolongations of the periplastic appendage.

The *calotte* gives the cell a pointed appearance.

FIRST SUBFAMILY.—Spirillaceæ (new family). Cells not flexible.

Genera. Spirillum and vibrio (of Migula).

SECOND SUBFAMILY.—Spirochætaceæ (new family). The cells are flexible.

First genus. Spirochæta (Ehrenberg). Cells without flagella, with a well developed periplastic appendix, and often showing an alveolar structure. Sometimes there are myonemes in the appendage. Types—*Spirochæta plicatilis* (*Ehrenberg*); *Spirochæta Balbiani* (provisionally).

Second genus. Treponema (Schaudinn). Cells with a flagellum at one and sometimes at both extremities, which is the prolongation of the sheath cap. A periplastic appendage has sometimes been demonstrated. Types: *Spirochæta buccalis dentium; Treponema pallidum.*

Third genus. Borrelia (new genus). Cells with peritrichial flagella. Type: *Spirillum gallinarium.*

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PROTECTIVE INOCULATION AGAINST PLAGUE.*

RICHARD P. STRONG, M.D.

(*Chief of the U.S. Government Biological Laboratory Bureau of Science, Manila.*)

The subject of immunization against pest is not only of general scientific interest, but to many tropical and subtropical countries is of great practical importance. One need only recall the mortality in India of nearly a million deaths from this disease during the year 1905 and of over one million during the first six months of the present year to be impressed with the significance of the problem.

It is true that the question of inoculation against plague has received considerable attention during the past few years, and that prophylactics have been recommended by several authors, but while it is admitted that by their use a certain degree of pest immunity can be produced and demonstrated in a number of the more insusceptible animals, and occasionally even in those very susceptible to this infection, nevertheless it has sometimes seemed questionable whether we were able by their inoculation to obtain in man an immunity of such a degree as to be protective against the natural and usual methods of infection of the malady.

In the latter part of the year 1903, when the Board of Health of Manila was practising among the Chinese of that city protective inoculation against plague by the injection of the killed cultures of the pest bacillus, the method at that time carried on in Japan and consisting of the injection of one oese of a twenty-four-hour slant agar culture of Bacillus pestis suspended and killed in one cubic centimeter of .085 saline solution, I decided to investigate whether any immune substances became developed in the serum of the inoculated individuals. It did not seem possible to me that any appreciable degree of immunity could be acquired from these

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inoculations, owing to the small size of the dose and the very mild local and general reaction which resulted from the injections; I therefore studied the agglutinative and bactericidal reactions of the blood serum of twelve cases, six of which had been inoculated two weeks, and six three weeks previously with one oese of the killed pest culture. The agglutinative reactions were performed by the macroscopic method, and the bactericidal reactions according to the one suggested by Neisser and Wechsberg. No traces of agglutinins or of specific bacteriolysins could be demonstrated in the sera of any of the individuals. (These experiments were undertaken at this time because the statement had previously been made that agglutinins, at least in some cases, had been demonstrated in the blood serum of human beings who had been inoculated against plague a short time before with Haffkine's prophylactic, a conclusion which I have not been able in any manner to confirm.) Obviously, these experiments in themselves were not considered to be conclusive evidence of the fact that no immunity was conferred upon the inoculated, since it was already recognized at this time that these anti-bodies were frequently and indeed, usually, not encountered even in the blood sera of individuals who had recovered from an attack of plague and were immune to this disease. (Experiments demonstrating the fact that animals immune to pest infection may still show no traces of agglutinins in their blood, together with those demonstrating the absence of a true bacteriolytic action of plague immune serum, will be presented later in this paper.) Therefore, experiments in animals were resorted to in order that more information on this subject might be obtained. Guinea-pigs were inoculated subcutaneously, each with the same dose that was being employed in the general human inoculations in this city. After two weeks the immunity of these animals was tested in the following manner: One oese of a virulent pest organism was suspended in one cubic centimeter of .085 saline solution and five loops of this suspension rubbed over a freshly shaved area on the abdomen of the guinea-pig. All of the animals succumbed to acute pest infection, demonstrating conclusively that an immunity of appreciable degree had not been produced.

A short time after, the important paper of Kolle and Otto[1] was published in which the unfavorable results from the immunization of guinea-pigs with large doses of killed agar cultures of the pest bacillus or with Haffkine's prophylactic were reported. It therefore seemed to me at that time more advisable to experiment further with other methods of immunization against plague before insisting upon the use of larger amounts of more virulent killed pest cultures in the human inoculations being pursued in Manila, further results obtained by Kolle and his associates having demonstrated that in very susceptible animals at least satisfactory immunization could only exceptionally be produced by the methods of human inoculation then in vogue. I recommended at that time to the Commissioner of Health in Manila a suspension of the human inoculations with killed cultures of the pest bacillus.

Methods of immunization studied. — A comparative study of the efficacy of the different methods of protective inoculation against plague was then undertaken and their value investigated not only in guinea-pigs, but particularly in the lower apes.

The argument has been advanced — perhaps justly — that the test of the value of a method of immunization for man against plague should not be judged alone by its action upon such animals as guinea-pigs and mice. Monkeys on the other hand suffer with all forms of pest infection analogous to those observed in man, and moreover are said sometimes to contract the disease naturally. In addition the limit of value of a method for the immunization of man against plague can probably better be studied in monkeys than in any of the lower animals, owing to the fact (as I have been able to demonstrate) that the behavior of these animals in relation to susceptibility and immunity much more closely resembles the behavior observed in man than it does the one seen in other lower animals. It was particularly for these reasons that the lower apes were extensively employed in my experiments in testing the final value of the methods of inoculation which had proved effective in the smaller laboratory animals.

The methods of immunization especially studied consisted of (1st) the inoculation of killed bouillon and killed agar cultures, (2d) of living attenuated cultures (that is of vaccination), (3d) of filtered cultures and extracts (free receptors of the organism), (4th) of artificial and (5th) of natural plague aggressin, and (6th) of the inoculation according to Klein's method. I may say in passing that in this paper I employ the term "vaccination" as implying exclusively an inoculation with the living attenuated organism.

These procedures comprise all those of importance which have been recommended for active immunization of man against pest, except that one described by Lustig and Galeotti. This method of extraction of the immunizing substances from the plague bacillus I have not employed, because it was believed that the other methods of extraction of these antigens which I used were somewhat more effective. Moreover, Kolle's experiments in immunization with Lustig's method did not lend any encouragement to its further use. The methods described in which serum was added to the killed organism before inoculation were also not extensively studied. Since my earlier experiments in cholera immunization had shown that when an immune serum was added to the killed organisms the immunizing power of the latter became reduced. Only when the living organisms are treated with the immune serum and inoculated does the combined method in plague become more efficacious.

It seemed desirable to experiment further with killed cultures of the pest bacillus for two reasons: First, to compare the immunizing value of the dead organism with that of other methods of inoculation such as those of vaccination, of natural and artificial aggressin injections, etc., and, second, to see whether sufficiently good results could be obtained by experiments on the lower apes to warrant advocating the use of this method in man.

The results of this comparative study of the value of the different methods have been recorded in detail in various papers during the past and present year, most of which have been published in the "Philippine Journal of Science" for 1906 and 1907.

These experiments have demonstrated conclusively and beyond any doubt the great value of vaccination against plague infection, and its evident superiority to the other methods.

Next in value to vaccination as a means of immunization against pest appear to be prophylactic inoculations of natural aggressin. Inoculations with artificial plague aggressin did not in my experiments prove to be nearly as efficient as those with natural aggressin. A much higher immunity was obtained with the latter prophylactic. However, as I have pointed out previously, there was apparently no difference in the quality of the immunity obtained with the natural aggressin from that produced by the artificial product, and my subsequent experiments, as did my earlier ones,[2] have only further confirmed the views of Wassermann and Citron[3] that the aggressins must be considered to be hypothetical substances and that, so far as their immunizing value is concerned, in these exudates we have to do mainly with the substances extracted from the bacilli themselves. Evidently, in the case of the plague bacillus, the receptors of the organism in the so-called aggressin exudates of animals become liberated in a more efficient manner for immunization and probably exist in a less altered condition than they do in the aqueous suspension of the bacilli obtained in vitro by artificial means. Obviously, in natural plague aggressin no other immunizing substances are existent than are present in the prophylactic against pest recommended by Terni and Bandi. The two methods are practically identical as Bandi[4] has recently pointed out.

However, it must be admitted that Bandi did not originally explain the principle of the action of his prophylactic, as we understand its action to-day after a study of the subjects of free receptors and aggressins.

However, the method of inoculation with natural plague aggressin is not likely to come into general use, because of the great difficulties encountered in the preparation of the prophylactic. Moreover, in my experiments I have not obtained the satisfactory results with it which Hueppe and Kikuchi[5] evidently anticipated. The method of *vaccination*, as already mentioned, gives a much greater degree of protection. Although Klein's method, according to the small number of experiments I have performed, gives about the same results in immunizing guinea-pigs as are obtained by the inoculations with natural aggressin, yet the injection of the former substance in my experiments produced a much greater local reaction than the latter. Therefore I could not ascertain that this method had any particular advantage over that in which inoculations of natural aggressin were employed.

Evidences of immunity from a study of the blood serum. — After having concluded from the experiments mentioned above that true plague vaccination (that is, inoculation with living attenuated cultures) produced the highest immunity, inoculations were made in human beings with a living culture designated as Pest avirulent. In order to ascertain if any evidence of immunity could be demonstrated in the inoculated, their blood was tested for the presence of agglutinins, anti-infectious substances, and opsonins. This led me to investigate in detail whether, and if so to what extent, these same anti-bodies existed in the blood sera of animals which had been immunized against plague infection.

Agglutinins. — From a large number of experiments I have concluded that the agglutinins are formed slowly and only in very small amounts in animals which are being immunized against pest infection and that they only occur in demonstrable quantities in those which have been very highly immunized. At most, only very minute traces of these substances are encountered after single inoculations of either the killed or the living organisms, no matter how large the dose which is employed. I am convinced that in my earlier experiments with plague agglutination I sometimes mistook pseudo-agglutinations of the pest bacillus for true ones, and from a study of the literature it seems to me probable that other observers have erred in this respect. A study which I have made of the blood sera of guinea-pigs which have been vaccinated against pest infection and which have later shown themselves to be immune to lethal and multiple lethal doses of the pest bacillus, has demonstrated that practically no traces of agglutinins exist in such sera. The same may be said of the sera of other animals immunized in a similar manner. Monkeys which have first been vaccinated with attenuated pest cultures or inoculated with killed cultures, and which afterwards have been shown to be immune to pest infection by the injection in increasing doses of from one-half oese to nearly one entire agar slant culture of a living virulent strain, still have developed in their sera practically no traces of agglutinins. Indeed, it is very difficult to immunize monkeys to such a high degree that the blood of the animals shows the presence of plague agglutinins. In a series comprising twelve monkeys in which an attempt was made gradually to immunize these animals with a strain designated "Pest Virulent" up to such a degree that the anti-bodies would be demonstrable in their blood, only two were able to survive the inoculations when the immunization had reached the point in which the agglutinins could be detected even in small amounts. The remaining ten animals succumbed either to pest infection or intoxication as a result of the injections, before agglutinins could be shown to exist in their blood. Moreover, notwithstanding the fact that from one-quarter to one-half oese of this strain "Pest virulent" represented a certain lethal dose for normal animals of this species, and although these monkeys were immunized to such an extent that in a number of instances they were able to resist and survive the inoculations of such large amounts as six to eight loops of this organism (over twelve times the maximum fatal dose), agglutinins were still not present in sufficient quantities to be demonstrable in their blood.

Only small quantities of agglutinins could be detected in the examinations of several pest immune sera which were prepared from horses and which were known to possess, in two instances at least, considerable protective (that is, anti-infectious) power.

A horse which was being immunized against pest, and which had acquired a sufficient immunity to withstand the injection of nearly ten agar cultures of a virulent pest strain, gave a serum which at this time showed an agglutinative reaction in dilutions of one to ten, but none above this strength. However, at the same time one cubic centimeter of this serum protected from fatal pest infection about sixty per cent of the white rats inoculated. A pest immune serum obtained from Asia, which protected about seventy-two per cent of the inoculated rats against fatal pest infection in doses of from one to two cubic centimeters, when carefully tested with the virulent pest strain showed no agglutinative reaction after three hours. However, it must be stated that at the time its anti-infectious and agglutinative reactions were tested this serum had been bottled for about a year. A second pest serum purchased from Asia, which showed a somewhat lower protective power, also revealed no agglutination when tested with the strain "Pest avirulent." This serum had been bottled about nine months. Moreover, a laboratory immune serum, which possessed a higher anti-infectious power and which protected about ninety per cent of the inoculated white rats against plague infection in doses of one cubic centimeter, also showed almost no agglutinative reaction against the virulent strain, giving only a weak reaction in a dilution of one to ten.

A study of the agglutinating properties in the blood of a number of persons who had been vaccinated against plague, as well as of several cases who had suffered with the disease and recovered, was also undertaken. In the majority of the instances no traces of agglutinins could definitely be demonstrated.

In concluding my remarks on agglutination it may again be emphasized that excessive precautions must be taken to distinguish between pseudo and true agglutination in pest, and that apparently only in the organism highly immunized against plague infection do the agglutinins become developed in sufficient quantity to be of any practical importance either in the diagnosis of the infection or in the demonstration of the presence of an immunity. It also would appear from my experiments that the development of the anti-infectious substances in a plague immune serum is quite independent of the agglutinins.

Anti-infectious bodies. — The method employed in investigating the presence of anti-infectious bodies in the serum was as follows: A rat was inoculated intraperitoneally or subcutaneously with the serum to be tested, while at the same time the animal was infected by thrusting beneath the skin near the tail a syringe needle which had been dipped in a suspension of a virulent pest organism. Numerous control animals were inoculated in all the series.

By numerous experiments of this nature it was demonstrated that the anti-infectious substances also become developed very slowly and in very small quantities in animals immunized against pest. While rabbits which have been given a single, small intravenous inoculation of either living or killed cholera or typhoid bacilli will develop a serum which in high dilutions is protective for guinea-pigs against multiple lethal doses of these organisms, on the other hand, rabbits which have been intravenously inoculated with large amounts of killed virulent or with living attenuated plague cultures yield sera which, when tested on rats, show apparently no protective power whatever against plague infection. Likewise, as large an amount as five cubic centimeters of a serum obtained from a rabbit previously inoculated intravenously with twenty milligrams of artificial plague aggressin proved to possess no anti-infectious power when tested on rats. Monkeys which had been immunized against pest by vaccination, or otherwise by inoculation, and which had been shown to be thoroughly immune by the subcutaneous inoculation of multiple lethal doses of the virulent pest strain, furnished sera which also showed no traces of anti-infectious power when tested on rats. Only in the case of one monkey could a slight anti-infectious power be noted, and this animal had received repeated increasing doses of virulent pest bacilli until it resisted the injection of one and one-half agar slant cultures of the living virulent pest strain. This series of experiments is particularly important because it illustrates that the negative results in the demonstration of an anti-infectious action, obtained with the serum of monkeys less highly immunized against pest, could not be ascribed to the lack of a suitable complement to complete the reaction in the body of the rat.

The sera of thirty-three human beings who had been vaccinated against pest by the inoculation of living attenuated cultures, and of a patient convalescent from plague were also tested, but in no instance showed any demonstrable anti-infectious value. However, since animals which had proved themselves thoroughly immune to pest infection also furnished sera which conferred no greater protection, it would not be reasonable to expect that the human sera would reach a higher power. Only in the case of horse's serum, where the animal had been finally inoculated with repeated large doses of living pest bacilli, could any marked anti-infectious action be demonstrated, and indeed with some of these sera it required as much as one cubic centimeter to save the rat from fatal pest infection. Therefore, it is unnecessary to emphasize further that the absence of the anti-infectious substances against pest in sufficient quantities to be demonstrated in a serum cannot necessarily be regarded as an evidence of the absence of even a considerable immunity against this disease in the individual in question, since in animals and human beings known to be thoroughly immune to pest infection it has also not been possible to demonstrate these protective substances.

Bactericidal substances. — My experiments relating to the study of the bactericidal action of the serum of animals immune to plague have been considered at length elsewhere, and will be summarized briefly here.

In conformity with the experiments of Kolle and Hetsch,[6] and more recently of Dean,[7] I[8] have found that plague immune serum which is known to possess anti-infectious power in the animal reveals in vitro no bacteriolytic reaction whatever that is similar to that possessed, for example, by typhoid immune serum. I have also been able to show that the pest bacilli are not only not killed after being treated with the immune serum, but that they remain alive and under some conditions are capable of subsequent development. However, that a reaction actually occurs between the plague immune serum and the bacilli is obvious from the further experiments of Kolle and Hetsch; these observers having showed that a binding took place between the amboceptors of the serum and the corresponding receptors of the bacilli, since after contact with the bacilli the serum was found to have lost in immunizing power. I have been able to confirm these experiments and in addition to show (loc. cit.) that in this reaction (binding of plague amboceptor and receptor) if fresh complement is present, it also enters into the reaction and becomes bound. My further experiments relating to the mechanism of the action of immune serum in vivo have showed in agreement with those of Markl[9] and Löhlein[10] that after the bacilli have been previously acted upon by the serum and prepared for the leucocyte the leucocyte ingests the organisms and plays a further part in their digestion and ultimate destruction, perhaps partly by furnishing the additional amount of complement necessary to complete the reaction. On the other hand, that the phagocytes in non-immunized animals do not to any extent engulf living virulent plague bacilli seems equally clear. Therefore the destruction of the plague bacillus is effected by the immune animal in a manner partly in accord with the humoral theory of Buchner and Ehrlich, and partly in accord with the phagocytic one of Metchnikoff.

Opsonins. — The action of plague serum may also be termed "opsonic" in nature, since it prepares the organism for phagocytosis. However, I have showed that the actual preparation of the bacillus, *i.e.*, the chemical change which it undergoes (in the instance of plague at least), consists of the binding of its receptors by the amboceptors of the serum, and of the union of complement in the serum, though obviously the entire phenomenon of what we have regarded as true bacteriolysis does not take place outside of the leucocyte.

Although the whole literature upon the question of the opsonic reaction cannot be entered into here, it may be mentioned that experiments in connection with this hypothesis have been further confirmed by those of Muir and Martin,[11] who have tested the three chief varieties of immune bodies and have found that in each case the combination of receptors plus immune bodies removes the opsonins at least of normal serum.

The work of Dean[12] and of Leidingham,[13] which has appeared since my experiments on this subject were first reported (March 2, 1907), although Dean had performed earlier work on this question,[14] also supports this hypothesis for opsonins of other sera. While the experimental work of Neufeld and Hüne[15] and the still more recent of Muir and Martin[16] on opsonins of immune serum is not in opposition to it in its most important features, the conclusions of these authors oppose somewhat this view. Neufeld believes that the action of the opsonin of normal serum is different from that of the bacteriotropin of immune serum. That the former consists of the action of amboceptor and complement, while the latter consists of the action of a thermostable substance, "Bakteriotropine Stoffe" which does not require the action of complement. However, to me it seems probable that in both instances the essential substance which prepares the bacilli for phagocytosis is a thermostable amboceptor. If a normal serum which contains but a small quantity of thermostable amboceptor is heated, obviously the complement is destroyed or converted into complementoid. If now the bacteria are treated with such serum and if the amount of amboceptor present in the serum is very small, the organisms remain unsensitized for phagocytosis, unless fresh serum containing complement is added to start the reaction. If on the other hand an immune serum which contains a large amount of thermostable amboceptor is heated and the complement largely destroyed and the bacteria then treated with it, the organisms become, nevertheless, sensitized for phagocytosis. For in the presence of a large amount of amboceptor but a small quantity of complement is necessary for the reaction, such as remains present, though altered, or which may be drawn from and furnished by the leucocytes. The question is particularly one of the quantitative relationship between complement and amboceptor, and particularly one of affinity of the amboceptor. This well-known phenomena was pointed out by Ehrlich, Morgenroth and Sachs several years ago.

Further, if certain immune sera, such as cholera and typhoid, which have earlier possessed bacteriolytic properties, and in which the complement has been converted into complementoid or destroyed, are added to their respective organisms, bacteriolysis obviously no longer occurs, unless fresh complement is added, but the organisms are, nevertheless, sensitized for phagocytosis. With such bacteriolytic sera it is either by means of a destruction or alteration of the complement or by diluting the amount of the amboceptor of the sera that the entire phenomena of lysis is prevented from occurring. The first stages in the reaction of bacteriolysis, nevertheless, take place, and the organisms are taken up by the leucocytes and later undergo destruction. The fresh complement when present in sufficient quantities quickens the rate of the reaction.

In plague serum both amboceptor and complement enter into the reaction of sensitizing the bacillus, for whose ultimate destruction usually the leucocyte is necessary. It seems probable that the morphological structure of this organism — its cellular membrane, capsule, etc., — afford it a certain protection against bacteriolysis, while free in the serum before ingestion by the leucocytes has taken place.

However, leaving aside the discussion of what this opsonic reaction in plague immunity exactly consists of, and whether it depends upon the action of new bodies or not, it may be stated that this reaction — at least sometimes — affords us a means of determining the existence of such an immunity, since I have been able to show that the blood serum of both human beings and animals which have been vaccinated and immunized against pest, frequently revealed an increased opsonic index, even though this was not invariably the case. The phagocytic power apparently varied somewhat according to the virulence of the organism employed in the test, the index usually being higher with the avirulent strain.

The technic which I have come to employ in determining the opsonic power of the serum is somewhat different from that which Wright recommends. In my experiments the leucocytes are always used in a perfectly fresh condition and obtained from the abdominal cavity of a normal guinea-pig after an intraperitoneal injection of aleuronat. They are kept at a temperature of 37° C. until the smears on the slides are prepared. Only very virulent strains of the pest bacillus were employed in testing the comparative value of the opsonic power between a plague immune and a normal serum.

In my earlier experiments the determination of the phagocytic power of the sera was arrived at in the usual way by attempting to count the number of bacteria in a certain number of cells and to divide the total number of bacteria by the number of cells counted. Later the errors which resulted in employing this method, in my hands, caused me to abandon it and to adopt the method of determining the highest dilution in which a given immune serum will give rise to a marked phagocytosis, and of then comparing its action with that of a normal serum in this same dilution. For example, when the organisms which have been treated with a certain serum in a fixed dilution undergo a marked phagocytosis, while the organisms of the same strain of bacteria treated with a normal serum in the same dilution undergo practically no phagocytosis, the opsonic reaction may be said to be increased in the former serum. While in the beginning of the work it was thought that the value of certain immune sera might be more or less accurately compared by this manner, it was soon found that the reaction was not sufficiently delicate for this purpose, and that only in those cases where one serum in a certain dilution gave rise to a very marked phagocytosis, and the other in the same dilution to practically no phagocytosis, could the opsonic reaction of the first serum be said to be increased.

Personally, I have not had any experience in attempting to determine the opsonic value of the serum in furunculosis and tuberculosis and of other infections where the nature of the resulting immunity is obscure We have no satisfactory method of testing the immunizing power of antitubercular and staphylococcus sera.

The work of Moss[17] and of Fitzgerrard, Whiteman and Strangeways,[18] which has recently been published, demonstrates conclusively the errors which may occur in determining by the counting method usually employed, the opsonic index in the same serum, and in other sera of practically the same immunizing power. Moss further showed that the sera obtained in rabbits by the repeated inoculation of killed and living cultures of Staphylococcus aureus possessed no greater opsonic power than normal rabbit's sera when tested by this method; while Fitzgerrard, Whiteman and Strangeways by their extensive work showed that with the usual technic no difference in the opsonic index could be shown to exist between the sera of healthy and of tuberculous human beings.

It seems to me regrettable that these same authors after having so carefully studied this technic with certain sera (staphylococcus and tubercular) did not pursue its study further in relation to those sera whose immunizing power and value have been definitely demonstrated by animal experiment.

Neufeld and Hüne have recently demonstrated the bacteriotropic reaction with typhoid and cholera immune sera, though the technic in determining what constituted an increased phagocytic power of the blood was different from that employed by Moss, Fitzgerrard and Strangeways.

Personally, I believe that the serum of the average tuberculous patient contains no immunizing power of demonstrable value; moreover, I believe it is not practicable to increase the immunizing power of such a serum to a demonstrable extent by a single small injection of killed tubercle bacilli, and certainly we have no proof that we can do so. I am inclined to believe it is only with living attenuated cultures that a valuable immunity against tuberculosis may be produced. However, the method of treatment with killed cultures is having an extensive trial, and the results obtained will doubtless shed further light upon this subject.

In connection with this work on immunization, one must not lose sight of the fact that it is largely through Wright's efforts, and the confidence in England and America, at least, which his work has aroused in the general public, that opportunity has and is being given to extensively and thoroughly test the value of inoculation with killed organisms in relation to the production of immunity in the treatment of various bacterial infections in human beings. While it seems probable that in many of these diseases no favorable results will ultimately be obtained, nevertheless the question may be decided definitely for each infection, provided that the experiments are sufficiently, extensively, and carefully performed.

Although some of us feel, and have shown that there are certain errors and limitations in the technic in determining the opsonic index as it has been employed, yet effort must be made to improve and place this upon a more satisfactory basis. While with some infections this may be difficult or impossible, nevertheless this need not be a reason in itself for the abolishment of the treatment of these various infections by inoculative measures. Care must be exercised not to bring discredit too hastily upon this method of immunization for the various infections, before it has been carefully and completely tested.

Deflection of complement. — Finally I have found that by means of the phenomenon of the deflection of the complement of Bordet and Gengou, we are also able to demonstrate in the serum the existence of an immunity against pest. This reaction has been carried on with the blood serum of vaccinated human beings and guinea-pigs and with horses' pest immune serum, as well as with normal human, guinea-pig, and horse serum. In each instance with the normal serum no deflection of the complement took place, while with the serum from the vaccinated individual and animals and with the horse immune serum, the deflection regularly occurred. All the necessary controls were performed and all the precautions in the technic of the experiments were taken. In spite of its many abuses, and all the objections raised against the method, in the hands of a competent bacteriologist it is the most delicate test we possess for the demonstration of the deflection of the complement.

In concluding the discussion of this portion of the subject, it may be stated that only by means of the deflection of the complement, and sometimes by the opsonic reaction, are we usually able to discover the existence of immune bodies in the blood serum of an individual or animal immunized to plague. The examination of the serum for agglutinative bactericidal or anti-infectious substances is usually of no practicable value in determining the existence of an immunity against pest infection, since agglutinins and anti-infectious substances are not present in sufficient quantities to be demonstrable even in animals which have been shown to be highly immunized against this disease and which have resisted multiple lethal doses of the organism, while the existence of true bacteriolytic substances cannot be shown to exist even in animals most highly immunized against plague.

The most satisfactory demonstration of the existence of plague immunity can be obtained from a study of the resistance of the animal to artificial infection, but such a test can obviously not be employed on human beings.

Human vaccinations. — The superiority of vaccination against plague having been shown conclusively by animal experiment, and other experiments[19] having demonstrated the entire safety of the inoculation of human beings with large amounts of the strain designated "Pest avirulent," more extensive vaccinations were made in man with this culture. The size of the dose employed for an adult was always one twenty-four-hour agar slant culture and for children from one-third to one-half of this quantity. Surprising as it may seem, the injection of these large amounts of the living plague organism have not given rise to any very severe reactions. A few hours after the inoculation the temperature of the individual usually begins to rise. When the injections have been made in the morning the fever may in the evening of the first day reach from 38.5° to 39° C. Only in a few cases has it touched 40° C. The temperature gradually declines on the following day, and by the third or fourth one has become normal. Occasionally, the cases showed a moderate leucocytosis after the injection. As in the earlier experiments, the organisms were always suspended in one cubic centimeter of .085 saline solution and the inoculations were made deeply into the deltoid muscle. Intramuscular instead of subcutaneous injections were performed on account of the quicker absorption which occurs from the former method, and because Meltzer and Auer found that intramuscular injections as regards absorption in general stand in value very near that of a direct injection into the circulation. On the day after the vaccination there is usually distinct induration and redness about the point of the injection, with soreness on pressure, but these symptoms, together with the febrile reaction, subside in from one to three days. No visible suppuration of the tissues has ever occurred.

In order to observe the length of time during which the organisms remained alive in the tissues, similar inoculations were made in monkeys and the tissues near the point of injection incised at varying intervals after the vaccination and microscopical preparations and cultures made from the drops of lymph and blood which escaped from the wound. In the different series of cultures made from the animals inoculated with the strain "Pest avirulent" it was found that from six to eight hours after the time of the inoculation the organisms were still very numerous in the tissues, after which time they gradually diminished, and, usually after twenty-four hours, they were no longer reclaimable in cultures. However, in several instances a few colonies developed in the cultures made after this period of time. In immunized animals the organism was destroyed in a short period, the cultures made after twelve hours frequently remaining sterile. In these instances smears from the tissues three or four hours after the inoculation showed very extensive phagocytosis of the bacteria. Therefore, the process of immunization occurs as in a true vaccination, the organism reproducing itself in the tissues for probably one hundred or more generations and its successive groups of receptors stimulating the production of corresponding groups of amboceptors in the animal body. It therefore is not difficult to understand why the immunity derived from vaccination in plague is greater than that obtained from the injection of the killed organism.

Although abundant evidence had been obtained of the resistance against plague produced in animals even more susceptible to infection than man (that is, guinea-pigs) by vaccination with these attenuated cultures, yet it was interesting to observe what evidence could be discovered, from a study of the blood serum, of the immunity resulting in human beings from such vaccinations.

The results of these investigations have already been referred to, and the evidences of the immunity obtained by a study of the opsonic reaction and the power of the serum to deflect complement emphasized.

Since my first report made upon the method of vaccination against plague in man, such inoculations have been made from time to time, and during the past year two hundred vaccinations have been performed. The cultures with which I have worked have so far proved themselves to be entirely safe for human beings, and I have observed no unfavorable results in the inoculated. However, as emphasized in my previous communication, vaccinations against plague should not be made in man unless the investigator can guarantee the particular organism which he is working to be sufficiently attenuated to be no longer dangerous for human beings. Strains of the bacilli which in extensive series of experiments, carried over long periods of time, invariably no longer kill guinea-pigs of two hundred and fifty grams weight upon subcutaneous inoculation, in amounts of one agar slant culture, are probably safe in small amounts for human beings. However, obviously each strain must be carefully and thoroughly tested before extensive inoculations in man are made with it. Moreover, one must always bear in mind that because a particular pest culture inoculated in a certain dose may have been demonstrated to be harmless for a small group of healthy and robust human beings, the conclusion must not be drawn that this same culture will always prove to be non-dangerous for individuals in poor health, and for those possessing a greater natural susceptibility to pest infection. The susceptibility to infection is so variable in different human beings that unless extreme caution is used in the selection of a proper culture, disastrous results are sure to follow. On the other hand, care must be taken to employ a culture which has been shown to be capable of immunizing against pest infection a high percentage of the guinea-pigs vaccinated with it.

Owing to the great stability in virulence of the plague bacillus under certain conditions, its use in vaccination is much simplified. During the past year and a half I have been able to detect no change either in virulence, toxicity, or immunizing power in the strains with which I have performed my vaccinations in man and in animals. The cultures apparently possess the same immunizing power to-day as they did at the commencement of the experiments. However, it is probable that they could be further attenuated by artificial means.

Douglas and Bullock (Allbutt and Rolleston's System of Medicine), in commenting upon my work in vaccination against plague, state that naturally very great care would be necessary in recommending a method like this on a large scale in plague-stricken communities, as from unforeseen circumstances the virulence might increase and plague be induced.

As I have pointed out, I have no evidence to support this statement and my cultures, which for nearly two years have been used at intervals in human beings, are as safe for use in man to-day as they were at the time of my first inoculations.

Nevertheless, cultures which are to be employed for human vaccination must be continually tested on animals to guard against the possibility of any such occurrence as that which has been suggested by Douglas and Bullock.

In discussing this question of vaccination in man against plague, with suitable cultures, I wish to emphasize the fact that the method is not infallible, and that very brilliant results may not always be obtained by it. In the vaccination ot large numbers of human beings, owing to individual variations in susceptibility to plague infection, and natural resistance, just as in numerous experiments performed with monkeys, certainly all of the individuals will not be protected against the usual lethal infection by a single vaccination with one agar culture, but we have proof that a good proportion of them may be immunized by this method, and an appreciable degree of immunity may be retained for at least ten or eleven months. The population in a plague-stricken district may gradually be immunized against this disease by the employment of vaccination.

In plague, as in small-pox vaccinations, it may frequently be necessary to repeat the vaccination, and perhaps with a larger dose, in order to secure a satisfactory immunity.

As yet we know of no practical method for the detection of those cases which would require a second plague vaccination to protect them from the natural manner of infection of the disease, and this subject requires further investigation.

In closing my remarks upon this subject, I shall summarize the work on protective inoculation against plague in the following conclusions:

1st. The usual hygienic methods which have hitherto been undertaken in combating plague in certain of its endemic centers, and from which there is continuous danger of invasion by the pestilence into other countries, have not always proved themselves to be effective. This fact is clear because the disease is not markedly decreasing in these centers. For example, India is at present suffering from an epidemic of plague larger than the one which occurred there in 1905. The official monthly returns from that country for the present year up to June, 1907, show 1,062,908 deaths from this disease. (These official figures have been kindly supplied me by Dr. Martin and Dr. Boycott of the Lister Institute, London.) The British Commission under the direction of Martin and Lamb by their recent important studies[20] have, moreover, demonstrated why the ordinary hygienic measures have failed and why they must continue to do so in the suppression of the epidemic.

2d. Following the earlier principles of Jenner in vaccination against small-pox, elaborated and extended by Pasteur to rabies, and certain other infectious diseases of bacterial origin, the German Pest Commission, consisting of Gaffky, Pfeiffer, Sticker and Dieudonnè performed experiments in the immunization of animals with living pest cultures, but owing to the difficulty of obtaining strains of sufficient attenuation, the method was abandoned. The Austrian Commission, Albrecht and Gohn, and the French investigators, Yersin and Carré, also employed pest cultures of moderate attenuation in the immunization of rats, guinea-pigs, and monkeys, and Yersin vaccinated himself cutaneously with a small amount of an attenuated culture. Kolla first conclusively demonstrated that in animals a higher immunity is obtainable by the use of attenuated plague cultures than by the inoculation of either the killed pest organisms or by Lustig's prophylactic. Finally, I have shown that by vaccination of animals with attenuated cultures not dangerous for inoculation in human beings a higher immunity can be obtained than by the inoculation of either the killed pest cultures or their extracts, including among them natural aggressin.

3d. While it is obvious for several reasons that for immunization in man in general, the inoculation of killed cultures or their extracts is far preferable and safer than the method of bacterial vaccination, nevertheless it would appear that in pest only by vaccination can a satisfactory immunity be obtained.

4th. While the attenuated cultures which I have employed in the vaccination of human beings have so far shown that their use in man is without danger, my work must nevertheless be considered as experimental, and more extensive experiments must be performed with different races and classes of people and under various conditions before the method can be recommended for general use.

The question which confronts us is whether we shall continue to combat plague by these measures which have shown themselves by ten years' experience to be entirely inadequate n the suppression of this malady in certain endemic centers, or whether we shall experiment further with a method which appears to offer us a greater hope of success in the suppression of this disease. Personally, I have demonstrated the value of the method of vaccination as far as it is possible for me to do so.

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AGAMOFILARIA GEORGIANA N. SP., AN APPARENTLY NEW ROUNDWORM PARASITE, FROM THE ANKLE OF A NEGRESS.[a]

By Ch. Wardell Stiles, Ph. D.,
Chief of Division of Zoology, Hygienic Laboratory, U. S. Public-Health and Marine-Hospital Service.

(Figs. 1–25.)

Eighteen specimens of a nematode worm (figs. 1–2) have been forwarded to this laboratory by Dr. St. Joseph B. Graham, of Savannah, Ga., with the history that they had been taken from a sore on the leg of a negress at Darien, Ga. All of the specimens are immature; they are not especially well preserved, and on this account they have presented considerable difficulty in technique and interpretation. Accordingly, it has been impossible to give a complete description of the species. But as the worm seems to be a new parasite for man, and as certain points in the anatomy could be recognized, it seems advisable to place the parasite on record, notwithstanding the fact that several important points are open to different interpretations and that the description is therefore necessarily incomplete.

Medical history of the case.—For the following medical history of the case I am indebted to Dr. P. S. Clark:

> In August, 1896, I was called to see a negress; age, 57; occupation, washerwoman. I found her suffering with pain and swelling in and around her left ankle and instep. She said she could feel something moving in the swollen places, but there was no abrasion on the skin. I gave her a linament with which to rub the affected parts. This did not seem to be of much benefit. She continued to suffer for twelve or eighteen months, when suddenly she discovered a worm coming out of the most swollen place; and worms continued to appear singly at intervals for a month, when the opening healed and the pain and swelling subsided, her foot became entirely well, and gave no further trouble. She died in 1903 of tuberculosis of the lung. I think there were as many as two or three dozen of these worms extruded from this opening during the above-mentioned period.

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[a] By permission of the Surgeon-General, and in response to an invitation, this paper was presented at the annual meeting of the American Society of Tropical Medicine, at Philadelphia, Pa., March 27, 1906.

Patient was never confined to bed as the result of the above condition. I preserved some of the worms in alcohol and gave them to my friend, Dr. Ralston Lattimore, of Savannah, Ga., as a zoological curiosity, who in turn handed them to Dr. St. Joseph B. Graham, of Savannah, who was kind enough to send some specimens to you for study and identification.

Systematic position.—The worms in question would probably be classified by many authors as a *Filaria.* Such classification is, however, not satisfactory, for in the absence of the adult stage it is difficult to determine to what group of the *Filariidæ* the parasites may belong. To place the species in *Filaria* would be adding confusion to an already very confused genus. Possibly these worms belong in *Tetracheilonema*,[a] but too little is known about the type species of this genus to justify a definite opinion.

As the most satisfactory solution of the systematic dilemma which presents itself, I propose to classify these parasites under the collective term—

AGAMOFILARIA new name.

Diagnosis.—*Filariidæ:* A purely collective group, to contain agamic forms of *Filariidæ*, which have not yet reached a stage in their development permitting of their being determined generically. Such a group has no type-species. Compare *Agamodistomum*, *Amphistomulum*, *Agamomermis*, *Merminthoidum*, *Agamonematodum*, etc.

As the species under consideration does not seem to be identical with any form described for man, and as it is not apparent at present that it is identical with any species described for other hosts, I propose to recognize it as a new species under the name *Agamofilaria georgiana*, with the following characters:

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[a] *Tetracheilonema* Diesing, 1861a, 621, 711 (Dec. 6, 1860) (m. *quadrilabiatum*).

Generic diagnosis.—*Filariidæ:* "Corpus longissimum, filiforme. Caput quadrilabiatum, labiis in quadrangulum dispositis. Os ad basin labiorum. Extremitas caudalis spiraliter torta. Penis vaginâ tubulosa. Apertura genitalis in anteriore corporis parte; uterus ——— Vivipara.—Avium brasiliensium in cavo abdominis et sub cute colli endoparasita."—Diesing, 1861a, 711.

The type species presents the following synonomy and diagnosis:

Tetracheilonema quadrilabiata (Molin, 1858) Diesing, 1861.

1858: *Filaria quadrilabiata* Molin, 1858, 417 (in *Tinamus rufescens*, at Caiçara; and *T. maculosus*, in Brazil).—Diesing, 1861a, 711.—Stossich, 1897, 77.

1858: *F. tinami* M. C. V., MS., in Molin, 1858, 417.

1861: *Tetracheilonema quadrilabiatum* (Molin, 1858) Diesing, 1861a, 711.—Stossich, 1897, 77.

Specific diagnosis.—*Tetracheilonema:* "Os quadrilabiatum, labiis conicis, magnis; corpus inflexum; extremitas anterior sensim attenuata; posterior spiraliter torta; extremitas caudalis maris attenuata, obtusa; vagina penis tubulosa, extremitate libera incrassata; penis ———; extremitas caudalis feminæ attenuata, obtusa. (Vivipara.) Longit. mar $1\frac{1}{4}$–$1\frac{1}{3}''$ [30 to 33 mm.]; crassit, $\frac{1}{3}'''$. Longit. fem., $1\frac{1}{2}$–$2''$ [36 to 50 mm.]; crassit, $\frac{1}{2}'''$.

"Habitaculum.—*Tinamus rufescens*, Novembri, Caiçara: in cavo abdom.—*T. maculosus*, in Brasilia: sub cute colli (Natterer). M. C. V."—Molin, 1858, 417.

AGAMOFILARIA GEORGIANA, new species.

(Figs. 1 to 25.)

1906: A new species of parasite in man, Stiles, 1906, Apr. 21, 839–840, N. York M. J. (1429), v. 88 (16); 1906, Apr. 21, 1232, J. Am. M. Ass., Chicago, v. 46 (16).

Specific Diagnosis.—*Agamofilaria:* Adults unknown.

Agamic form: Length 32 to 53 mm. Body cylindrical, of more or less uniform diameter the greater part of the length, with a maximum diameter of about 560 to 640 μ; gradually attenuated toward both extremities, slightly more gradually cephalad than caudad. Mouth terminal, central, circular, small, unarmed, but surrounded by six papillæ. Four of these are prominent, submedian, 23 μ elevations, having in some cases almost the appearance of lips; two smaller papillæ are latero-median. Anus a transverse slit, about 44 to 56 μ in transverse diameter, situated ventrally, 64 to 128 μ from end of tail. Tip of tail provided with a small conical projection 8 to 13 μ long by 4 μ in diameter. Excretory pore 0.432 to 0.520 mm. from anterior end. Cuticle in general without transverse striation, except for a fine transverse striation in the anal region, especially postanal, and a (probably pseudo-) striation in the esophageal region. Median lines visible externally in glycerine specimens merely as lines of demarcation between the muscular fields; on section, median bands are very slender, but are visible, and extend centripetally below the muscles, widening in breadth. Lateral bands rather prominent, and may be traced practically the entire length of the worm; they may attain a breadth of 96 μ, but they decrease in breadth cephalad (to about 15 μ) and caudad; they are divided into a dorsal and a ventral portion, which are not necessarily symmetrical and which are separated by a distinct line of single, subcuticular cells; the cells of the lateral bands are chiefly subcuticular, but near the head they extend centripetally in a single row in each half. Attached to the lateral bands, and hanging into the body cavity each side is a sinuous, longitudinal ridge, resembling the head-glands of strongyles, and provided with a central longitudinal canal which empties at the excretory pore; in the bridge of the esophageal region this glandular structure possesses a large apparently unilateral nucleus (296 to 316 μ by 90 to 132 μ), situated latero-ventrally. Esophagus simple, 2.5 to 2.9 mm. long, 88 to 114 μ in diameter (anteriorly) to 334 μ in diameter (posteriorly); its lumen is triradiate, each ray measuring about 10 μ. Chyle intestine straight, or very nearly so, rather large, at first compressed laterally, then rather quadrangular, with fibers running from the submedian lines toward the body wall; farther caudad it becomes flattened dorso-ventrally, measuring about 300 μ transversely by about 200 μ dorso-ventrally; its cells are columnar, about 9 μ in diameter by 30 to 90 μ high; the cuticle of the lumen is about 6.6 to 8.8 μ thick. Rectum about 200 μ long. Body cavity almost completely occupied by the intestine, lateral, longitudinal glands, and a reticular structure extending centripetally from the muscles toward the intestine; a considerable amount of granular material also present (? some of this possibly representing the primordium of the genital glands).

Habitat.—Agamic form taken from superficial sores on the ankle of a negress (*Homo sapiens africanus*), at Darien, Georgia, U. S. A. Life history and source of infection known.

Type Material.—U. S. P. H. & M. H. S., No. 9726.

The following details were observed:

GENERAL EXTERNAL CHARACTERS.

Size.—The worms (figs. 1–2) vary in length from 32 to 53 mm., the eighteen specimens giving the following measurements: 32 mm., 34 mm., 36 mm., 37 mm., 38 mm., 40 mm., 42 mm., 45 mm., 47 mm., 49 mm., 50 mm., 52 mm., and 53 mm.

In the longest specimen (53 mm.) the cephalic extremity is bluntly rounded; 80 μ caudad of the mouth it is 128 μ in diameter; it swells gradually to 368 μ in diameter a short distance caudad of the posterior end of the esophagus.

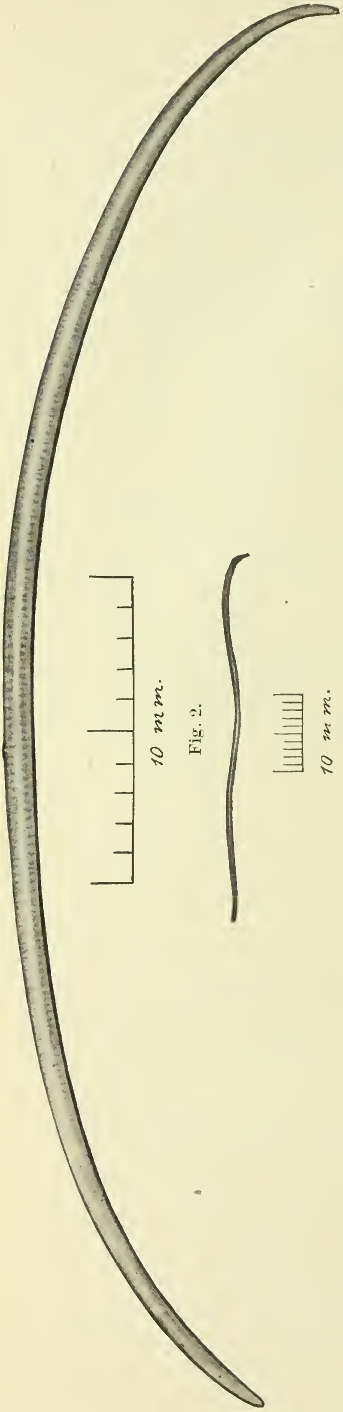

Fig. 2.

Fig. 1.

Fig. 1.—*Agamofilaria georgiana* from ankle of a negress at Darien, Georgia. Natural size.

Fig. 2.—Specimen of same, enlarged 4 times.

In the specimen 44 mm. long, the diameter is 160 μ at a point 80 μ back of the mouth; the maximum diameter is 560 μ.

In the specimen 37 mm. long, the diameter 80 μ back of the mouth is 136 μ; at 800 μ back of the mouth the diameter is 272 μ; 1.6 mm. back of the mouth the diameter is 368 μ; the increase is then rather gradual, and at the end of about the first third of the specimen the diameter attains 560 μ; then a diameter of 576 μ is retained more or less uniformly, but with a slight variation, at some points reaching 624 μ; toward the tail, the diameter begins to decrease, at first slowly, then more rapidly; at 1.6 mm. from the tip, it is 400 μ; at 800 μ it is 272 μ (dorso-ventral diameter); at the anus the dorso-ventral diameter is 120 μ; the tail then ends rather bluntly.

In a mounted specimen 32 mm. long, the diameter 80 μ back of the mouth is 128 μ; at 800 μ it is 240 μ; just before the end of the esophagus it is 432 μ; just back of the esophagus there is a slight constriction, to 400 μ; it then varies between 560 and 640 μ for the greater part of the length; near the tail it begins to decrease, reaching 432 μ at a point 1.6 mm. from the tip; it now decreases more rapidly, reaching 240 μ at a point 800 μ from the tip; at the anus, the dorso-ventral diameter is 80 μ.

In general, the body may attain a maximum diameter of about 560 to 640 μ and is more or less uniform for a considerable part of its length; it tapers gradually toward both extremities, the attenuation toward the head being slightly more gradual than that toward the tail.

Torsion of the body.—These specimens present a torsion around the longitudinal axis, so that when the head is viewed dorsally, the anus of the specimen is shown in profile; when the specimen is so placed on a slide as to give a ventral view of the anus, the head is seen in profile.

Head.—The head (figs. 3–5) is rather bluntly rounded, without any indication of a cephalic cone. The small terminal, central, circular mouth is surrounded by six papillæ, which are directed forward.

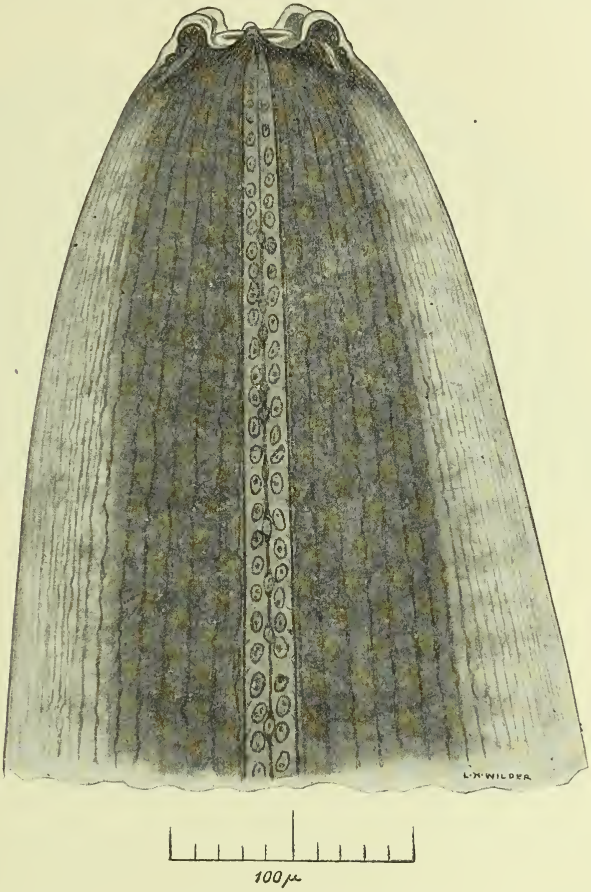

Fig. 3.—Head of same; greatly enlarged lateral view, showing the mouth surrounded by two small lateral papillæ and four larger submedian lip-like papillæ; note the lateral line with its two distinct rows of nuclei (one dorsal and one ventral), and a third, middle row of less distinct nuclei separating the others; note also the longitudinal striation due to the somatic muscles; the darker field is caused by the underlying esophagus.

Two of these papillæ are small and latero-median. Four of the papillæ are submedian and are much larger than the latero-median papillæ; they bear some resemblance to lips, and frequently show a larger, clearer portion, situated closer to the mouth, and of more lip-like appearance (fig. 4), and a smaller, darker, external ridge, which appears of more distinctly papillary nature; from base to tip these larger lip-like papillæ measure about 23 μ. There is some variation in the specimens, due possibly to their condition, which makes it difficult to infer just how these papillæ would appear in perfectly fresh or in well-preserved material. Extending caudad from the more strictly papillary portion (the external ridge), in several cases structures were seen which were strongly indicative of nerves.

Cervical papillæ have not been observed.

The *excretory pore* is small, medio-ventral, not prominent, 0.432 to 0.52 mm. from the anterior end.

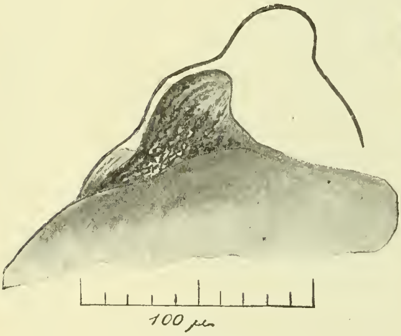

Fig. 4.

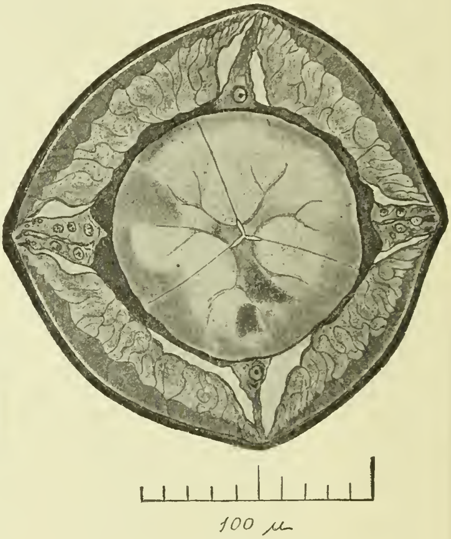

Fig. 5.

Fig. 4.—Greatly enlarged profile view of one of the submedian lip-like papillæ, showing the lip-like projection near the mouth and the external papillary portion.

Fig. 5.—Enlarged transverse section of head, close to the mouth. Note the following points: The cuticle seems to present two layers; it shows thickenings near the lateral lines; immediately under the cuticle, the thin subcuticula is visible as a light line extending around the body; at the four longitudinal lines (dorsal, ventral, and two laterals) the longitudinal bands are seen, extending toward the esophagus, and connected by a circular bridge which surrounds the esophagus; the lateral bands are thicker than the median bands, and present a dorsal and a ventral half; each half shows a row of nuclei; besides these a single middle nucleus is seen; the muscles are divided into four quadrants by the longitudinal bands; centripetally of the more darkly colored contractile muscular layer the protoplasmic processes extend toward the esophagus, forming a mesh work; the esophagus is central and shows a triradiate lumen and radial symmetry.

Tail.—The profile of the tail (figs. 7–9) is not uniform, but it bends slightly ventrad. In one mounted tail the transverse diameter at the anus is 128μ; in one mounted tail the dorso-ventral diameter at the anus is 80μ; and in one unmounted specimen, the dorso-ventral diameter at the anus is 120μ. In these three specimens, the anus is 96, 64, and 80μ, respectively, from the tip of the tail; in two other specimens it is 104μ and 128μ, respectively, from the tip. The anus is a transverse slit about 44 to 56μ in transverse diameter.

At the apex of the tail, there is a small conical projection, 8 to 13.4μ long, 4.4μ in diameter; this may be curved slightly dorsad and is not equally prominent in all specimens.

CUTICLE.—The cuticle at the anterior portion of the body is not so thick (about 3μ) as that (about 4 to 6μ) over the greater part of the worm (measurements taken from sections and also from worms). In general it shows no transverse striation; at the tail, however, quite a distinct but fine striation is visible in the postanal portion and in one specimen these striæ may be followed cephalad to the plane of juncture of the rectum with the chyle intestine; some of the specimens also show a transverse striation in the esophageal region, but this is probably a pseudostriation, as it is not constant and as it is most prominent on one specimen in which the head is rather strongly curved.

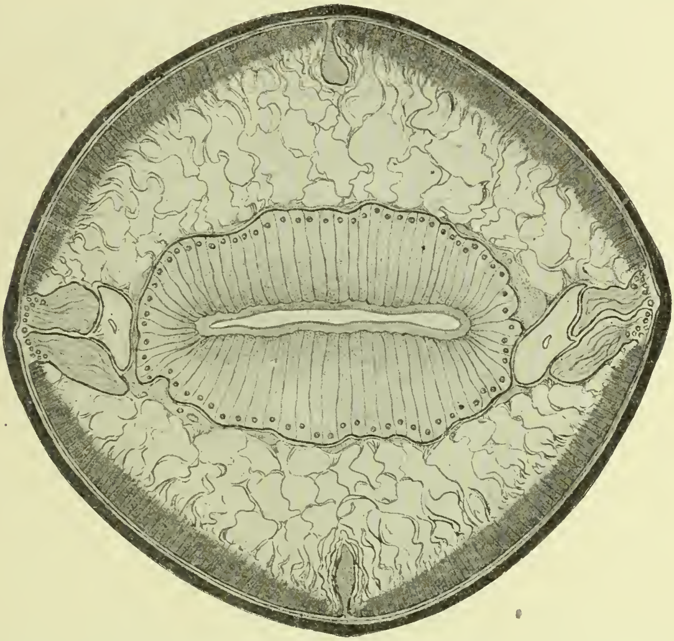

FIG. 6.—Enlarged transverse section of body through midgut region. Note the following details: The cuticle appears in two layers and presents four distinct thickenings, two near each lateral line; the subcuticula is visible between the cuticle and the muscles; the narrow dorsal and ventral median bands extend into the body cavity beyond the muscle layer and then increase in breadth; the division of the lateral bands into a dorsal and a ventral half is very distinct; near the cuticle, in the space between them, is seen a nucleus; nuclei are also visible in each half near the cuticle; the four muscular fields and the centripetal reticulum are very evident; the intestine is compressed dorsoventrally, and presents a high columnar epithelium with centrifugal nuclei and centripetal cuticular lining; between the lateral bands and the intestine is seen, each side, a section of the excretory gland, with its central canal.

A distinct longitudinal striation is visible upon microscopic examination; this is due, not to any striation in the cuticle but to the longitudinal somatic muscles.

Longitudinal lines.—The lateral bands are prominent, but externally the dorso- and ventro- median bands are barely recognizable; the position of the latter may, however, be distinguished externally, midway between the lateral bands, as longitudinal lines, at which the somatic muscles are thinner than usual, and in fact at which the respective muscle cells are slightly interrupted; the median lines may, however, be described as practically invisible externally; on section they are seen to be very narrow centrifugally, but slightly broader centripetally.

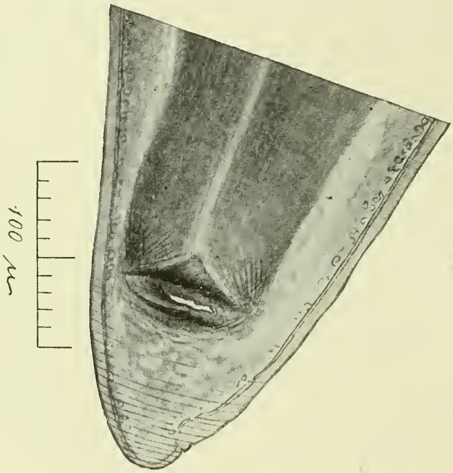

Fig. 7.

Figs. 7–9.—Enlarged ventral (7) and lateral (8 to 9) views of the tail. Note the transverse striation in the post-anal portion; the broad transverse anal slit; the midgut is large, but the rectum is compressed dorsoventrally; the lateral band, with numerous nuclei, is prominent; various cells, nuclei, and muscles are seen.

Lateral bands.—The lateral bands may be traced the entire length of the worm, from a point immediately back of the latero-median papillæ at the anterior end to the end of the tail; in the esophageal region they are somewhat less distinct than in the midgut region. Very close to the mouth, in one specimen, the lateral band measures 15μ broad and shows two distinct and one rather indistinct row of nuclei directly under the cuticle; sections, however, show other nuclei farther away from the cuticle; in one section very near the mouth, the band measured 13.2μ dorso-ventrally; the band increases gradually in breadth; at the posterior end of the esophagus in one worm it measures 45μ; in one specimen, it is 56μ and in another specimen 88μ at this point; at the equator of the worm it measures 90μ; it retains this breadth more or less uniformly to within a short distance from the anus, when it gradually decreases in actual breadth, although it may increase in relative breadth, owing to the decrease of the dorso-ventral diameter of the worm. The greatest breadth of the lateral band noticed in any specimen was 96μ. In one specimen it measured 30.8 at the anal plane.

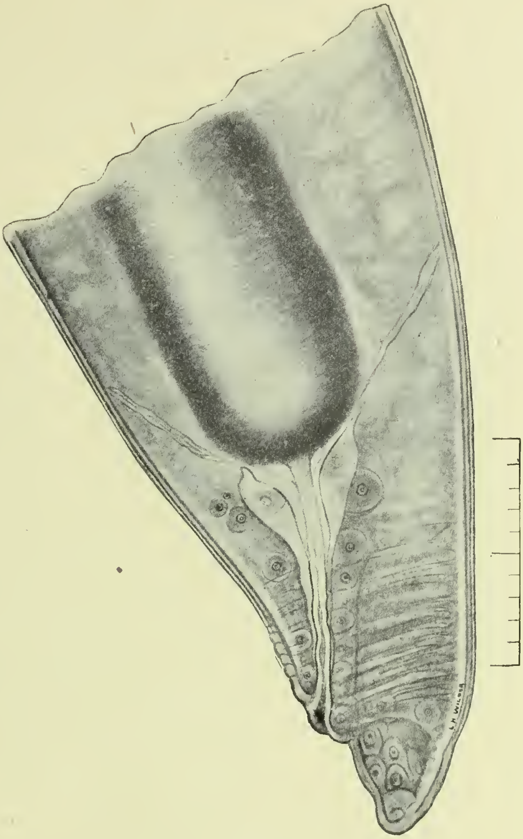

Fig. 8.

INTERNAL STRUCTURE.

Not an inconsiderable amount of the anatomy can be seen in specimens cleared in glycerine, but for an interpretation of some of the structures sections are necessary.

Digestive system—The intestinal canal consists of three distinct portions: a long undivided esophagus; a long chyle-intestine (midgut), and a distinct rectum.

Esophagus.—The esophagus (figs. 5, 10, 11, 15) is 2.5 to 2.9 mm. long; anteriorly it is 88 to 114μ in diameter; caudad it increases in diameter, at first slowly, then more rapidly, attaining its maximum (about 334μ) slightly in front of its caudal end. The measurements of the esophagus vary in different specimens. No differentiation into the dispharagus type was observed. A torsion of the esophagus is present. In its caudal half and at some other points the esophagus lies more or less exactly in the middle axis of the body, but portions of its anterior half may be decidedly excentric, nearing the dorsal surface of the worm. On section the outline is circular, but the lumen is seen to be triradiate, each leg of the 3-rayed star measuring about 10μ. The body of the esophagus (figs. 5, 11) presents an exceedingly interesting arrangement of its component parts, but because of the poor condition of the material it is perhaps better not to attempt a definite interpretation at this time. It may, however, be stated that nuclei are visible at some points and that at other points there are structures which are indicative of nerves and of glands; further, that the component parts of the esophageal wall present an almost mathematically exact radial symmetry, the three chief fields of the symmetry being determined of course by the three legs of the triradiate lumen; finally, the component parts

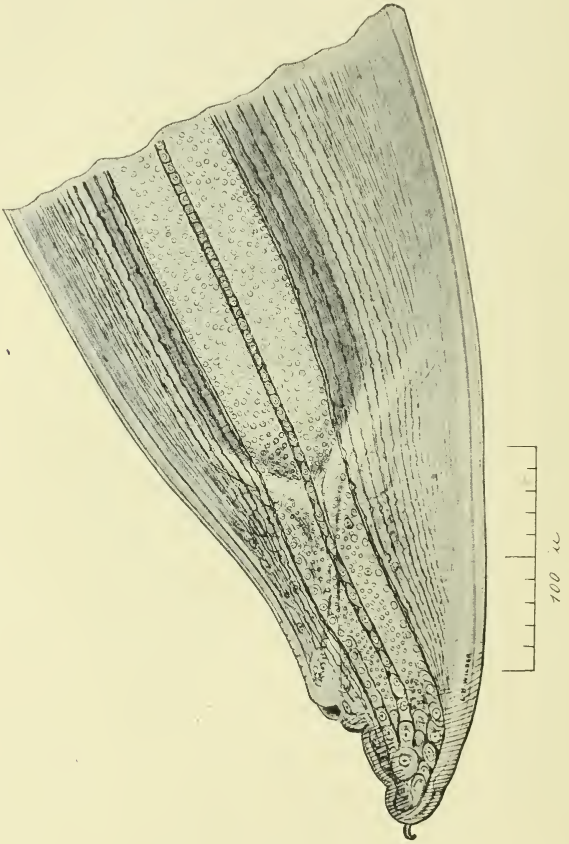

Fig. 9.

of each of these three fields present a more or less exact symmetry. The esophagus is more or less surrounded by certain structures, which will be described farther on.

Chyle-intestine.—The chyle-intestine or midgut (fig. 13) is of nearly uniform diameter and runs straight from the posterior end of the esophagus to the anterior end of the rectum. Focusing upon the chyle-intestine through the body wall, one distinctly sees the bases of the intestinal cells; they are about 9μ in diameter and arranged much like the cells of a honey-comb.

Viewed in transverse section the chyle-intestine is seen to be at first somewhat compressed laterally, then it becomes rather quadrangular, near the esophagus, but farther caudad it becomes somewhat flattened dorso-ventrally, so that its lateral diameter is about 308μ to a dorso-ventral diameter (closed lumen) of 202μ. The lumen is suppressed, or nearly so, and contains no food; the high, cylinder-epithelial cells are about 9μ broad; those near the median line are longer (in some cases attaining about 90μ) than those near the sides (which may decrease to 30μ); the nuclei of these cells are arranged near the distal end, namely away from the lumen, and measure about 6μ; the cells themselves contain numerous particles, apparently representing reserve food material;

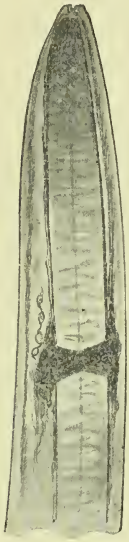

Fig. 10.

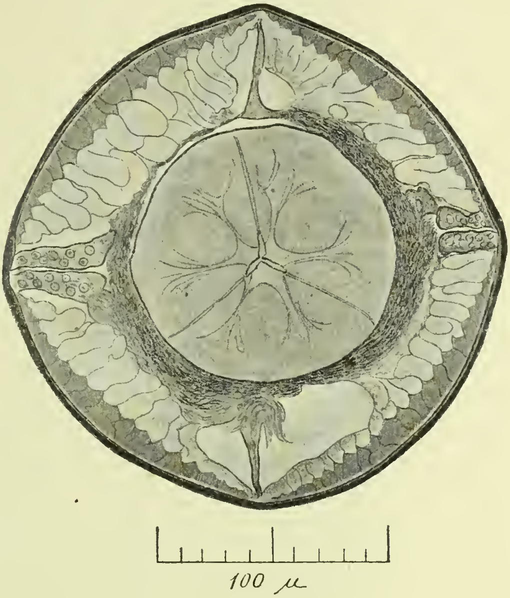

Fig. 11.

FIG. 10.—Enlarged view of the head, showing the central nervous system; the crossed condition of the fibers was quite evident in one specimen, but compared with other specimens this point in the drawing is somewhat exaggerated and diagrammatic.

FIG. 11.—Transverse section of head through region of the central nervous system. In addition to the characters described for fig. 5, note that instead of a bridge connecting the four longitudinal bands, there is a distinctly fibrillated structure which represents the central nervous system.

the cuticle of the lumen is 6.6 to 8.8μ thick, and in the posterior portion of the midgut this cuticle may show a rod-like structure. In the anterior quadrangular portion of the midgut, fibres run from the submedian corners toward the body wall.

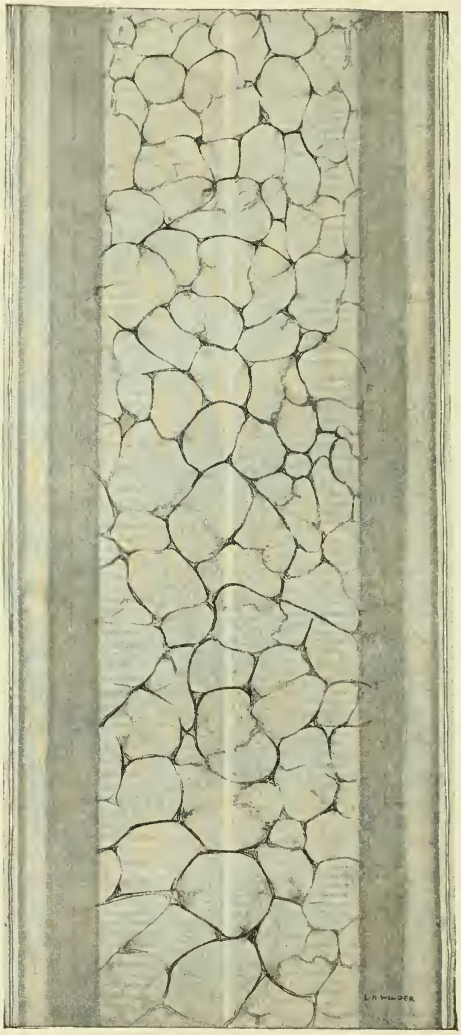

FIG. 12.—Enlarged view of a midgut portion of a worm cleared in glycerine, as seen dorsally or ventrally. Note the following characters: The clear line in the middle represents the median line or band; near this is seen a fine mesh work which represents the surface view of the intestinal epithelium, as seen upon deep focus; above is a much coarser network, which represents the surface view of the reticulum (compare fig. 6) between the muscular layer and the intestine; the broad band, occupying more than half the figure, is the intestine; laterally of this there is on each side a dark band, representing the excretory glands; lateral of these are the areas of the lateral bands, with their nuclei; then the subcuticula, and finally the cuticula.

Rectum.—The rectum (figs. 7-9) is about 200μ long. Several large nuclei are visible in this region, and certain cell boundaries can be distinguished, but the details were somewhat unsatisfactory, owing to the condition of the material.

Nervous system.—The brain (figs. 10–11, 15) surrounds the esophagus at a plane corresponding rather closely to the excretory pore,

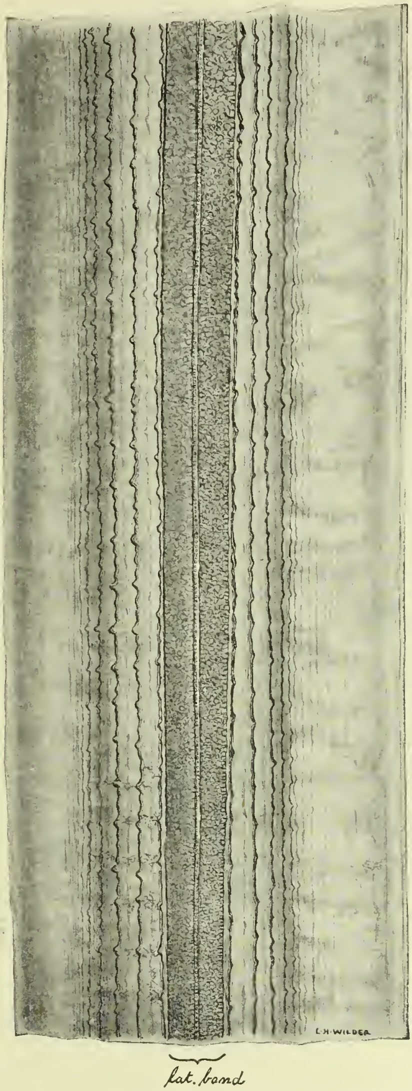

Fig. 13.—Enlarged lateral view of a midgut portion of a worm cleared in glycerine. Compare this with fig. 12, and notice the following details: The dark field in the middle is the lateral band (enlarged still further in fig. 14); this shows two parallel halves (dorsal and ventral), separated by a middle row of cells; the wavy, more or less parallel lines represent the somatic muscles; near the sides of the figure one obtains a lateral view of the large reticulum shown in fig. 12; on deep focus, this reticulum is, of course, much more distinct than can be shown in a view drawn in perspective.

namely, about 416μ from the anterior extremity. There is some slight variation in the different specimens, so that this measurement is somewhat diagrammatic and corresponds to an excretory pore 432μ from the cephalic end. A few cells, evidently ganglionic in nature, could be distinguished in the brain, but a detailed description of them would be difficult and rather unsatisfactory on the present material. Likewise a detailed description of the nerves would be likely to lead to errors of interpretation until fresh material can be found. It may be mentioned, however, that in one specimen in particular the fibers of the nerve ring seem to cross, as shown somewhat diagrammatically and in slightly exaggerated condition in fig. 10. At the submedian papillæ, and also in some other parts of the body, structures were observed which were strongly indicative of nerve elements, fibers, and ganglionic cells, but it is thought best not to describe them here and thus to avoid a danger of error of interpretation.

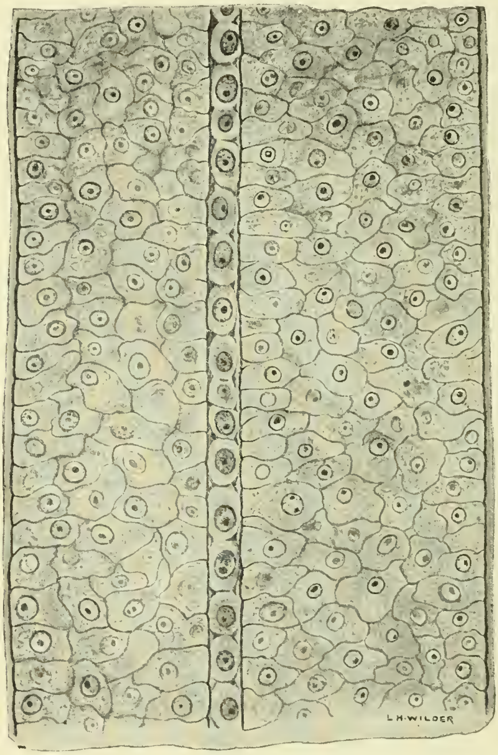

Fig. 14.—Very greatly enlarged lateral surface view of the lateral band of a specimen cleared in glycerine. Note the two halves (dorsal and ventral) of the band separated by a distinct line of cells; note also the nuclei and cells.

Muscular system.—On examination of mounted specimens cleared in glycerine a marked longitudinal striation is visible on certain focus. This striation, rather wavey in character in many places, represents the somatic muscles. On transverse section (figs. 6, 11–14) these muscles are seen to be arranged in four distinct quadrants, separated from each other by the four longitudinal lines. There are about 15 to 20 fibers per quadrant at about the cerebral plane, but in the equatorial plane there are many more—70 or more. These fibers are evidently quite long, but their length was not established. On cross section it is seen that the fibers in the submedian lines present the greatest radial diameter, while those nearer the longitudinal bands are smaller. The striation of the fibers is chiefly tangential to the worm, although occasionally a peripheral radial striation is noticed. The contractile substance of any given quadrant presents a notched or serrate appearance on its proximal border, and from the top of the teeth of the serration centripetal fibers are noticed extending toward the intestinal tract. These centripetal fibers bound the protoplasmic processes of the muscle cells and form a mesh work which almost completely fills the body cavity and which gives a very striking picture as one views a mounted specimen cleared in glycerine. Because of the direction of the mesh work the dorsal and ventral views (fig. 12) of the worm, in respect to this mesh work, are entirely different from the lateral view (fig. 13). The superficial meshes are smaller than those which lie more deeply. The entire picture, as seen through the body wall, reminds one of adipose tissue. On transverse section, however, it is seen that fine fibers proceed from the apices of the serrate border of the muscular layer; these fibers extend in a general way toward the intestine, but in an irregular course. Approaching each other, they form small meshes near the muscle fibrillæ, with larger meshes toward the intestine. The smaller meshes near the muscle fibrillæ contain a finely granular mass; the larger meshes may be clear or nearly so. Nuclei may be observed here and there in the mesh work.

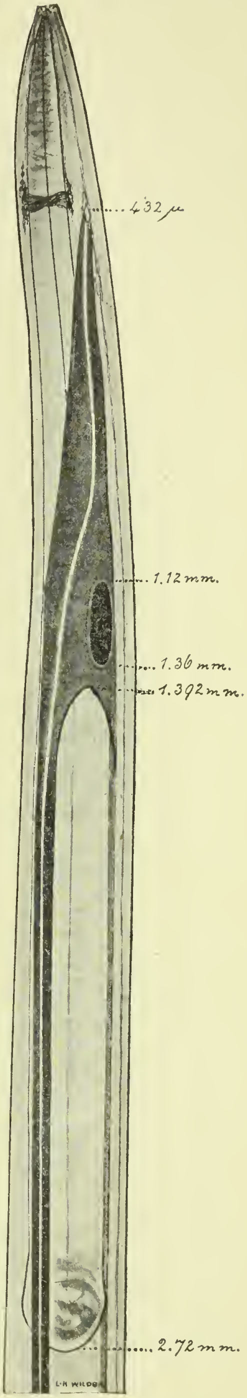

Fig. 15.—Enlarged ventro-lateral view of esophageal region of a specimen cleared in glycerine, very slightly diagrammatic. The esophagus is 2.72 mm. long; the brain is situated 0.416 mm. from the anterior end; the excretory pore is immediately ventro-caudad of the brain; from the pore a canal can be traced on the non-nucleated side of the bridge; the two excretory glands dip ventrally and unite ventrally of the esophagus; laterally and somewhat anterior of their point of union, an enormous nucleus (240μ long) is visible; no canal is drawn on the nucleated side of the bridge. The measurements on the right give the distance of the points in question from the head.

LONGITUDINAL BANDS AND SUBCUTICULA.—As stated in the foregoing, the lateral bands are much more highly developed than are the median bands; further, the lateral bands are in close relation to the excretory glands, so that the two together present an appearance which one is at first tempted to consider as indicating a common origin. Closer study, however, indicates a more distinct separation than at first seems probable.

Subcuticula.—The subcuticula is very thin, but in some sections, and even in some worms cleared in glycerine it appears quite distinct.

Median bands.—The median lines can be distinguished on most sections (figs. 5, 6, 11). In most sections the median bands are seen to extend as very narrow structures centripetally beyond the muscle layer and then to become broader. In the esophageal region, especially anterior of the brain, they are more distinct than in the midgut region, and immediately back of the mouth they are connected with the lateral bands to form a suspensory bridge around the esophagus (fig. 5).

Lateral bands.—The lateral bands are much more complicated in structure than are the median bands. Very close to the mouth they are rather narrow (figs. 3, 5), extending centripetally, however, nearly to the esophagus. They may be more or less distinctly seen to be composed of two portions, one ventral, the other dorsal; each portion is supplied with distinct nuclei; farther caudad this division into a dorsal and a ventral portion is very apparent. Anteriorly, where the band is narrow, a lateral view of specimens cleared in glycerine shows two rows of nuclei directly under the cuticle—one row in the dorsal, the other in the ventral portion; on cross sections of this region not only are these two subcuticular nuclei visible, but in each portion a row of nuclei (fig. 5) is seen extending toward the esophagus.

Beside these two rows of nuclei, a third, at first less distinct, row of single subcuticular nuclei (figs. 3, 5) appears situated between the two more distinct rows and separating them; farther caudad, as will be shown below, this middle row becomes more distinct.

Centripetally of this middle row some sections seem to present a delicate but distinct longitudinal canal between the two (dorsal and ventral) halves of the lateral band. Whether this is an actual canal, as is indicated by the sections, or whether it is an artifact due to the material, may possibly be better left an open question for the present, for there are some sections in which the canal is not distinct, while in some sections which are torn the tear corresponds to this apparent canal. The sections in question can hardly form the basis for a strong argument against interpreting the structure in question as a canal, for the latter is a delicate structure, the lumen of which might easily be suppressed at some points, while any tear of the section would rather naturally occur at this point.

Farther caudad, for instance in the midgut region of the body, the lateral band presents a very striking appearance (figs. 13, 14). On examination of specimens cleared in glycerine the lateral view shows broadened dorsal and ventral halves, in which a distinct subcuticular cellular structure is evident; each cell presents a nucleus. While these nuclei are seen at almost any point, they appear more distinct and more regular near the margins of each half. The middle single row of cells becomes very distinct, separating the dorsal and the ventral halves of the band.

Sections (figs. 16 to 25) confirm the surface views, and show certain additional characters. There are two quite distinct thickenings of the cuticle at the lateral band, near the lateral line. The dorsal and the ventral halves of the lateral band are seen to vary considerably in transverse outline as sections are followed caudad, and the two halves are not symmetrical, one to the other. The nuclei are seen to be more massed and more numerous near the dorsal and ventral margins of each half than between these points; most of the nuclei are situated centrifugally (distally), but here and there nuclei are found some distance proximally (away from the cuticle); further, cellular prolongations are seen to extend centripetally, toward the proximal margin of the lateral band; in some cases these cells were followed nearly or quite to the proximal margin; in some sections there appeared to be a decidedly distinct differentiation in the proximal (centripetal) portion,

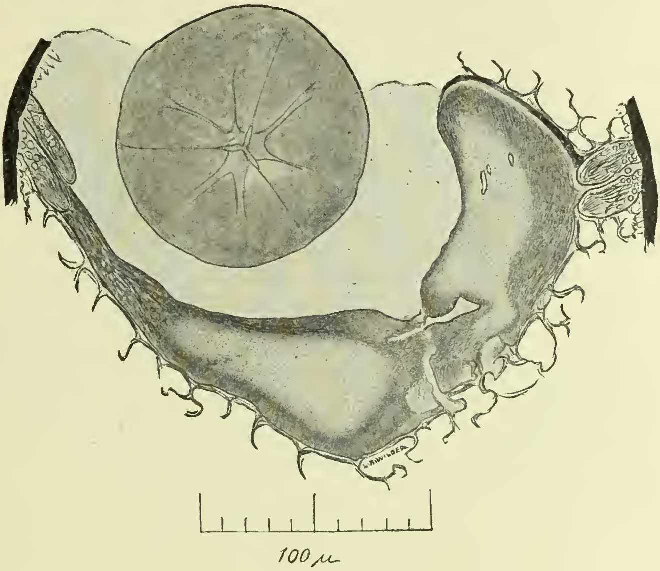

Fig. 16.

Figs. 16–25.—Nine transverse sections of the lateral band and the excretory gland in different parts of the body, except that figs. 19 and 20 and figs. 21 and 22, represent the two glands on opposite sides of the same cross sections. Fig. 16 is anterior of the nucleus and shows a bladder-like widening (*ex. c.*), apparently belonging to the excretory canal. Fig. 17 is through the nucleus. Note the excretory canal (*ex. c.*) on the nonnucleated side. Dorsally of the nucleus is a thick-walled canal-like structure. The nucleus is somewhat contracted from the nuclear membrane. Fig. 18 is a section caudad of the point of union of the bridge. Figs. 19–20 show the two lateral bands and two glands from one section. Note their asymmetry. Figs. 21–22 show the two lateral bands and glands further caudad. Fig. 23 shows a section in which the gland has reduced in cross section and exhibits a reticular structure. Fig. 24 shows a section still farther caudad. Fig. 25 shows a section near the caudal end of the gland. The latter is very small.

indicative of a lack of distinct cellular structure; whether this differentiation was an artifact, and more apparent than real, due to the condition of the material, may better be left for decision when fresh material can be examined. The dorsal, ventral, and proximal margins of each half of the band present a condensed appearance which in not a few sections is indicative of a distinct membrane.

Toward the lateral line, corresponding to a frontal plane of the worm, the dorsal and ventral halves of the lateral bands are distinctly separated. This separation is due primarily to the single, middle row of cells mentioned above. The nuclei of these cells can be very distinctly seen both on surface views and on section, but it is more difficult to trace the centripetal portion of the cells themselves. In some sections the cells could be quite distinctly followed to the proximal borders of the two halves of the band, namely to the point at which the gland (to be described below) meets the marginal point between the two halves of the band. The picture obtained was strongly indicative of an interpretation that the middle row of cells in question acted as a connective element between the gland and the subcuticula. Such an intrepretation was not confirmed, however, by some of the sections, for the cell could not be traced to the proximal margin, and the space not occupied by the cell appeared not unlike a canal; the possibility is by

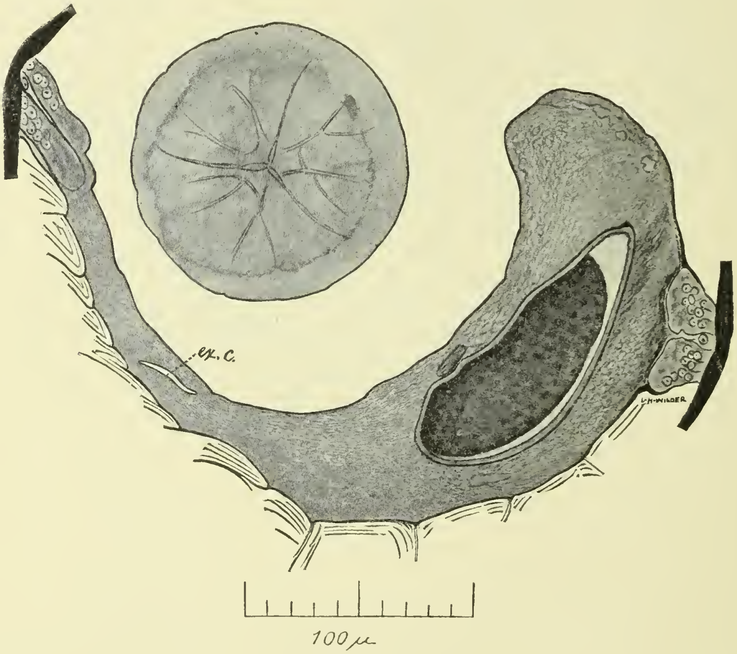

Fig. 17.

no means excluded that this canal-like appearance was an artifact; in fact, certain sections strongly indicated that it was. In still other sections, the middle cell was rather short, but a process from the large gland could be followed centrifugally between the dorsal and ventral halves of the band, nearly or quite to the middle cell.

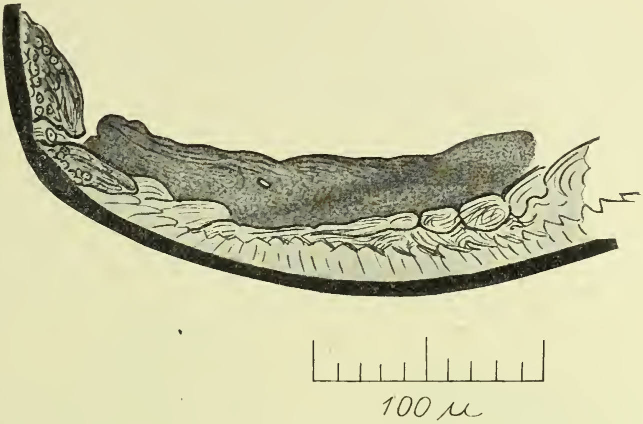

Fig. 18.

The determination of the existing conditions must be left for study of fresh material, notwithstanding a strong indication on some surface views of the existence of a longitudinal canal with a lumen of about 4 to 6 μ in diameter.

Excretory system.—The excretory system is very striking, but only a part of it can be interpreted at present.

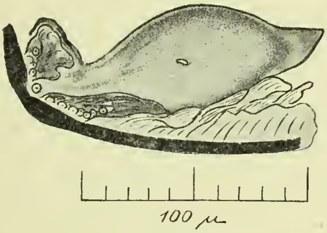

Fig. 19.

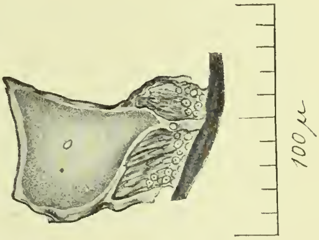

Fig. 20.

On surface views of worms cleared in glycerine a large, longitudinal ridge, of somewhat sinuous outline longitudinally, is seen on each side of the body, in close relation to the lateral bands. On transverse sections several prominent characters of this ridge are distinctly visible. In the first place it is seen that in any given section the transverse outline of the two ridges may be entirely different (compare fig. 19

with fig. 20, and fig. 21 with fig. 22); this fact is easily explained by the sinuous character noticed on surface views. Independent of this variation between the two ridges of any given transverse section, there is a marked difference in the transverse outline of the gland in different parts of the body. This outline is to some extent correlated with the transverse outline of the lateral bands, for, in general, when the bands are low radially the gland is likely to be large, while when the gland is small the bands are likely to be larger radially. The gland may be followed into the posterior portion of the body, where it becomes very small; toward the esophageal portion of the body, it becomes larger and more prominent.

Another point visible on transverse section is the presence of a distinct canal in about the center (axial line) of each gland; although some sections were found in which this canal was not distinguishable, it was distinct in so many sections that its existence can hardly be questioned.

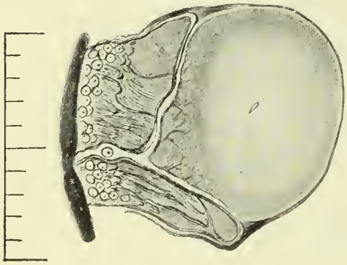

Fig. 21.

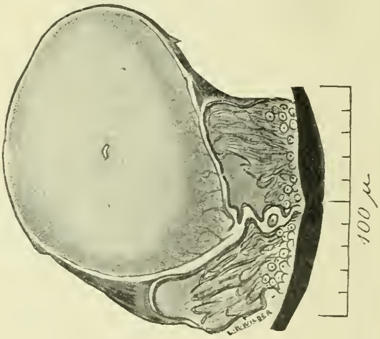

Fig. 22.

In some sections, the gland appeared granular, in others it was more distinctly reticulate in appearance.

Surface views of the middle (equatorial) esophageal region (fig. 15) show that the two longitudinal glandular ridges dip ventrally and unite to form a bridge; the united structure can then be traced cephalad nearly or quite to the excretory pore; one canal also is seen to dip ventrally and can be traced to the excretory pore; the natural expectation is that the two canals (one from each side) unite before reaching the pore; on surface views the point of union was not recognized. On sections the excretory pore was confirmed; almost directly dorsally of it were at least two (possibly several) cells, each with a distinct nucleus; tracing the excretory canal caudad it is seen to possess for a short distance a rather thick cuticle; suddenly the wall becomes thin and the canal *seems* to broaden into a larger cavity resembling a bladder (fig. 16); several of the following sections are unsatisfactory, but the canal can be traced on the nonnucleated side (see below) of the bridge until it reaches the vicinity of the lateral bands, corresponding to what was observed in two worms cleared in glycerine (fig. 15). On the nucleated side of the bridge the study was less satisfactory, but dorsad of the nucleus a thick walled canal-like structure was observed in several sections (fig. 17).

On surface views a large, distinct, and rather remarkable nucleus is also visible; this is situated slightly cephalad of the point of union of the glands and appears to be unilateral; at least, in no specimen, either on surface view or in section, could two such nuclei be distinguished. This fact, that only one nucleus could be found, is strongly indicative of an interpretation that the two glands together represent in reality only one cell. As the nucleus found was very distinct, it is difficult to assume that the absence of a second nucleus was due to the condition of the material.

This nucleus varies slightly in shape, but, in general, it is much longer than broad; it may attain a measurement of 296 to 316μ long (parallel with longitudinal axis of body) by 90 to 132μ broad (transverse to longitudinal axis of body). Both in mounts of the entire worm and in sections, the nucleus presents a thick nuclear membrane and a content of exceedingly large granules. Its appearance is very suggestive of the large nuclei of the cephalic glands of *Agchylostoma duodenale* (see especially Looss, 1905, figs. 5 and 38).

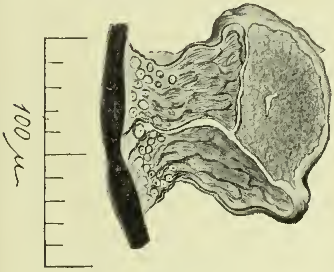

Fig. 23.

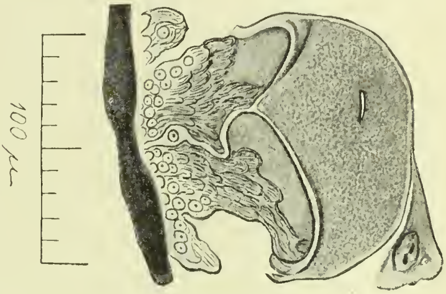

Fig. 24.

From the foregoing description it will be seen that the glandular structures do not correspond closely, so far as could be observed, with the conditions described by Looss (1905) for *Agchylostoma duodenale.* While recalling the unsatisfactory condition of the material, it is seen that no true distinct systems of cephalic and cervical glands have been observed, and that what would seem to correspond to the head glands of *Agchylostoma duodenale*, judged from their position in respect to the lateral bands, and from the large nucleus, appear to discharge through the excretory pore; further, that the two sides of the animal are not symmetrical in respect to these structures. Further study is, of course, advisable on material in better condition.

The ridge does not necessarily extend directly at right angles to the median line of the lateral bands, but may fall toward the median surface lines of the body; thus, in an examination of a worm mounted whole, one may focus superficially upon the margins of the true lateral band and then more deeply upon the displaced margin of this ridge; such change of focus gives an impression that the lateral band is broader than it really is.

A *longitudinal canal* may be seen in transverse sections of this ridge. This canal can be traced on sections caudad practically to the caudal end of the ridge; in tracing it cephalad, some sections were found in which the canal could not be distinguished with certainty, but in the majority of the sections it was visible.

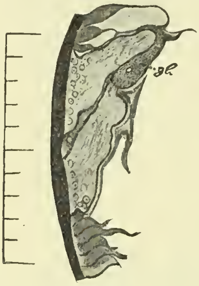

Fig. 25.

Even from this rather incomplete description, it is seen that the ridge is not an integral part of the proliferation of the subcuticula which forms the lateral bands *s. str.*, but rather an organ of glandular appearance, reminding the observer of the so-called cephalic gland, described in certain nematodes.

Genital organs.—In no specimen were structures found which could be positively interpreted as representing genital organs. One would naturally assume that in an animal of this size there must be such organs present in at least an early stage of development. Probably they are present, although they could not be recognized.

Body cavity.—The body cavity is almost completely occupied by the intestine, lateral ridges, and the mesh work extending inward from the muscular layer. In addition to these structures a considerable amount of more or less coarsely granular material was found; in at least one instance a granular structure (? ? primordium of the genital organs) was found unilaterally, close to the lateral band near the posterior end of the chyle intestine.

Reprinted from the New York Medical Journal for October 19, 1907.

A PARTIAL RESUME OF THE PROPHYLAXIS OF TROPICAL DISEASE.*

(*Published under the Imprimatur of the American Society of Tropical Diseases.*)

By J. H. White, M. D.,
New Orleans,
United States Public Health and Marine Hospital Service.

Having in mind the trite saying that the speaker should say something that he knows, say it briefly and stop, and realizing fully that any attempt to cover the whole or any considerable part of the subject assigned me, would be prolix, I shall confine my remarks to the subject of yellow fever prophylaxis, after barely touching upon leprosy and plague.

Leprosy.

The present status of our knowledge of leprosy compels the statement that the only prophylaxis which can avail anything is the enforcement of existing quarantine laws, under which most nations forbid the landing of a leper on their soil under any circumstances, and demand the complete segregation of all lepers already within their borders. The uncertain period of incubation renders any other measure of precaution an absurdity from the start.

Plague.

The prophylaxis of plague presents for study more of practical interest because more can be accomplished, but even here we deal with a question which is only sporadically presented to us in America.

The findings of Major Lowson, of I. M. S., in Hong Kong, that his English employees addicted to the use of soap and water and the wearing of shoes

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* Read before the American Society of Tropical Medicine, June 7, 1907.

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and puttees, escaped scot free, though daily handling bubonic plague, and that of our own workers in San Francisco, Kinyoun, Blue, M. J. White, and Kellogg, to the same effect, point rather strongly toward personal cleanliness and freedom from abrasions of lower extremities as the best of prophylaxis against this variety, while the readiness with which any one receives infection from the pneumonic form is still stronger evidence of the theory that plague must needs enter by either a skin abrasion or a delicate membrane, and not through the sound skin. Again, the puttee protection indicates the flea and gives us a clue to our line of procedure, which is to destroy rats and fleas in any plague spot or on any ship leaving such spot.

The small vitality of the *Bacillus pestis* itself makes our task, as far as the bacillus is concerned, relatively easy. The tremendous vitality of the flea is probably the greatest difficulty we have to encounter, not even excepting the danger of conveyance through dessiccated rats that can only be disinfected by burning.

The application of an absolutely safe quarantine against plague is practically impossible because it would mean the destruction of commerce, and no system capable of practical application is or can be absolutely effective so long as stupidity or venality exist.

Regarding practical quarantine, we should consider that a vessel thirty days out from a plague port is probably not infected, unless something has appeared on board during the voyage, to indicate plague. Should, however, any case have occurred, we must not permit such a vessel to touch the shore until we have destroyed her infection, and to this end we use four per cent. sulphur dioxide gas for a period of at least twelve hours, to insure the destruction of all animal life, and subsequently cremate the remains thereof.

Dealing with plague on land, it has been found that washing down rooms with a 1 to 1,000 solution of bichloride of mercury, followed by sulphur, and this, in turn, by white wash and by full and free ventilation and sunning, wherever possible, is most effective, although in many instances nothing seems certain of success. Haffkine's and Lustig's inoculations are effective, but hard to introduce, except through force, with the very class needing them, and our experience in California prompts the statement that for contacts, Yersin's serum, and for others, straight personal cleanliness, is, after all, the ideal personal prophylaxis.

Yellow Fever.

With the advent of the white man in the west began his four century war with *yellow jack,* and it must be confessed that the dominant race among men has been badly worsted, and until 1900, seemed in a fair way to remain worsted.

No unknown enemy can be successfully combatted, and the whole world owes a debt of gratitude to Reed, Lazear, and Carroll, because, through the work of this immortal trio, we know how yellow fever is transmitted and have more than a hint as to the nature of its specific cause. It would be a fitting capstone to the monument of fame already erected in our hearts to them, if the surviving member of the Commission could crown his life work by laying bare the exact causative agency.[1]

Knowing its method of transmission to be through the mosquito, we can, with the aid of the following facts as to the nature of the insect and the local conditions confronting us, indicate our line of procedure:

1. The stegomyia breeds generally in artificial containers.
2. It prefers clean water, although, under com-

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[1] Dr. Carroll has died since this paper was written.—AUTHOR.

pulsion, that is to say, in the absence of clean water, it may even utilize a cesspool.

3. It has been classed by Dr. Howard as a really domesticated animal, and is distinctly a house mosquito that cannot stand the glare of the sun.

4. It thrives best in a humid climate.

5. It has no inclination to travel, and, while undeniably doing so, it is always as a matter of accident, her migrations, *as a rule,* being limited to feet rather than to miles.

6. It is almost certainly an exotic, and ought to be with absolute certainty, an exile.

Here an apparent digression is necessary in order to state certain facts leading up to certain deductions.

The people of our south coast are environed by atmospheric humidity, and this, with long summers, fosters a riotous growth of insect as well as vegetable life.

Those cities of the south which have been most often the victims of yellow fever are those in which there is no notable altitude above the sea level, and which have deficient drainage, and New Orleans, be it known to those who have not observed it for themselves, is, for a portion of the year, actually below the river level, and all of her sewage and her vast area of surface drainage must, of necessity, be pumped out day by day. Having only a very limited supply of potable water, other than that furnished by the inevitable cistern, some 70,000 of which are to be found within her limits; with mud streets, many of them grass grown, flanked by 750 miles of open sewers and providing in damp weather, an ideal harboring ground for the mosquito; with a cosmopolitan population accustomed to the widest possible latitude of individualism and prone to resent any interference by the authorities with what they conceive to be their personal rights; with no effective means of compelling the report of cases unless the physician in attendance considers them to be yellow fever, New Orleans offers, from the standpoint of yellow fever elimination without regard to any other matter, a striking example of natural disadvantages. The Public Health and Marine Hospital Service at the inception of its work in 1905 in New Orleans, was confronted with no less than 616 known cases beside widely scattered but undoubtedly existing unknown cases, impossible to locate at the outset, and making necessary a general destruction, so far as human means could accomplish it, of all mosquitoes of the particular variety mentioned, it being, in the nature of things, impossible to locate all the infected mosquitoes after an epidemic is in full swing.

With such facts as these in mind and noting the vastness of the task of mosquito extermination, it seems that prevention of ingress of yellow fever to such localities is for the present imperative, and to this end we must continue to quarantine and must carry the war into Africa.

Beginning at the tropic port which we suspect of infection, where by a fumigation with even so little as one per cent. sulphur dioxide, applied simultaneously in all the parts of a vessel just before sailing, we destroy all mosquitoes, and, doing so, destroy all risk in so far as the ship itself is concerned.[1]

Then let us suppose that we renew our risk by taking passengers or crew from the infected port and that one of these is stricken on the voyage.

If, then, there are no stegomyiæ aboard, there is no transmission, but in the exceptional case in which some may have hatched aboard, one or more of these might become infected through biting the patient during the first three days of illness. Here our margin of safety lies in the fact that for about twelve days the infection is latent, and before that time expires our ship will reach a quarantine, even if the master is so ignorant as not to destroy the mosquitoes himself.

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[1] According to Francis, of the United States Public Health and Marine Hospital Service, an even smaller percentage of sulphur is entirely effective if the sealing is carefully done.

On arrival at quarantine our authorities, after seeing that all openings were sealed so that no mosquitoes were driven out rather than killed, would fumigate with sulphur very thoroughly, remembering that we are now where a mistake might produce deplorable results. Finally, when the one hundred and thirty-seventh hour incubative period has elapsed since the last possible exposure of each and all, let them go.

When a ship arrives at her wharf after leaving quarantine, you naturally suppose that this is the end of prophylaxis—but not so. In the case of any ship from the tropics, we must know the health status of her personnel six days after she sailed, as otherwise some *accidental infection from an unsuspected port* might be let loose on the community.

Regarding detained ships, experience shows that ships under surveillance are never the bearers of disaster. It has always been borne by those from a supposedly clean port. The essential point is that *the personnel of all ships from all tropic ports should be kept under observation to complete six full days.* This is difficult, but can be done, and if a system of giving each passenger a modest rebate check on his passage money, to be honored upon presenting himself to duly constituted health authorities, could be put in effect, the number unfound on final inspection would be less than one in ten thousand. As it is now, experience justifies the statement that our own citizens can be relied upon very nearly to that extent, and even among foreigners we find less than five per cent. to give wrong addresses, and less than one half of one per cent. of the total personnel covers those whom we cannot find at all, as against an estimated five per cent. lack of efficiency in ordinary methods.

In actual practice the inspecting officer meets the ship and identifies each passenger on landing, so that if correct addresses are given, there can be no failure later. This system, except the rebate check, is by order of Surgeon General Wyman now in operation in New Orleans and Mobile, and it is to be desired at all points.[2]

Now let us suppose that all of our precautions have been evaded; that there is a broken link somewhere in our chain, and that we find ourselves confronted with an outbreak of yellow fever so well established that the origin of many cases is obscured. Then we must resort to such measures as the following:

A thorough organization if not already existent is a prerequisite to good work, and must be had at once. The essential parts of such an organization are:

1. A central office in touch with all parts and provided with a perfect record system so that every detail may be referred to at a moment's notice.
2. Division officers under the command of competent executives to personally direct the work and provided with a force of intelligent workers sufficient in number to cover the division fully, at least once a week.
3. A school of instruction in detail work of mosquito destruction.
4. All employees should be trained to act in squads of three or four, and the proportion of untrained to trained men in any squad should, so far as possible, be held down to one in three, and in this kind of work more than in any other known to me, the master's hand must be ever on the helm. The division chief must be sleepless in his vigilance, for nothing short of absolute efficiency will attain promptly, the end in view.

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[2] Since this address was delivered the State of Texas has adopted this system, and Dr. Brumby is working in hearty cooperation with the Service.

Now we will consider the actual working details: Upon the announcement of a case, either actual or suspected, the whole house preferably, but the sick room certainly should be screened against the ingress of mosquitoes to be infected, and the egress of those infected.

A room should be prepared by carefully screening doors and windows, pasting up cracks and fumigating with sulphur and, the patient's condition permitting, he should be removed thereto at once and the whole house fumigated in all its parts, to insure the destruction of all mosquitoes.

The fire places and chimneys become harboring points, and the latter should be closed at the top before fumigation, in order to kill, *not drive out,* any insects therein. The screeners and pasters must be quiet as well as effective in their work, and in doing it they must neither drive the mosquitoes out, nor disturb the patient. In this connection I wish to pay tribute to Professor A. L. Metz, of Tulane, who, in 1905, proposed and organized and taught so thoroughly a training school for screeners, pasters, and fumigators that these men learned to do their work, even such as was necessary in the sick room itself, without complaint against them by either family or physician.

After the patient recovers sufficiently to move about, which is generally within the twelve days required by the infection to become dynamic, it is then wise, as an extra safeguard, to again fumigate the whole house.

Just here it is fitting to say that experience fully justifies the assertion of Dr. Carroll, that in dealing with yellow fever outbreaks, the best (and only reliable) policy is to treat all cases of fever as worthy of suspicion. There is no doubt that under such a plan thousands of unnecessary disinfections will be done, but it is, if you will pardon the paradox, just as necessary as any other part of the work as long as it is true that no man can always be relied upon to make an exact diagnosis in any disease, wherein the causative entity is not definitely known. We must not wait for a definite diagnosis, but disinfect first, and then await the leisure of the family physician, who will sometimes make, after this disinfection, a diagnosis he dared not make before. This is not intended to be ill natured, it simply means that there are black sheep in every fold and some spineless men in every profession. We all know this, and we want facts, not flattery. Of the "ninety and nine good sheep which went not astray," we need say nothing here.

Now let us turn to the wider field of the general destruction of mosquitoes in all cisterns, tanks, rain barrels, cesspools, tubs, buckets, old bottles, street and roof gutters, catch basins, water closets, tanks, and bowls, and even such unsuspected places as the church fonts and cemetery vases. Each and all must be sought out at regular intervals of not more than five days, and covered with a thin film of petroleum, or salted up to five per cent., or treated with cupric sulphate, or *emptied and dried*, simple emptying does not fill the requirement. If 150 degrees kerosene is used, it will not damage drinking water in any way, and a very mild solution, 1 to 200,000 cupric sulphate, will not injure vegetation.

Doing this we arrest reproduction by closing every avenue to the breeding ground, even the occasional ones like the cesspool and gutter to which the insect might resort in the absence of clean water. Coincidentally we should, wherever possible, enlist the sympathies of the public in the interest of a wholesale destruction of the living insects by a general fumigation, but a word of caution is due just here, against allowing the public to gather from this the idea that they can or will be trusted to do for themselves the special fumigation which must be done in actual cases of fever, and done with such absolute accuracy as will guarantee that all the insects are shut in and exposed for a time minimum of two hours to a volumetric minimum of two per cent. of sulphur dioxide. This must not even be entrusted to the family physician.

We must officially fumigate every house, the premises of which are contiguous to those infected, both for the furtherance of the good work of general destruction, and as another of those extra precautions which are always in good taste in this work.[3]

Special officers should periodically inspect every water container in the whole community, and harsh though it be, the penalty for the presence of larvæ in any container should be the discharge of the employee whose duty it is to keep that particular spot in order. Other officers should make house to house visitations to ascertain the presence and character of any sickness; not to see the sick, but in order that the central office may get in touch with the family physician.

The ingress and egress of persons to and from the city must be watched, and to lesser extent, the vehicle of egress. Incoming persons may be absolutely controlled by the means heretofore suggested, and if such means were universally adopted it would, of course, render egress comparatively safe for the outside towns, provided no person known to be from an infected house, was allowed to depart.

Reference to vehicles now brings us to one of the most interesting phases of this discussion, which is the extent to which the *Stegomyia callopus* travels, as well as the circumstances under which she does so, and, finally, what is to be done. We must not reason from analogy with other species and be led into error, because others do travel. The stegomyia is domesticated and may be justly likened to the quiet

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[3] Mosquito extermination is most effective if so timed as to catch the late autumn crop of larvæ, and oiling persisted in till the insects stop laying. This prevents October eggs to hatch in April, and is more potent for good than ten times the same work at any other season.

Swiss peasant, while the *Culex solicitans* is like the wandering Bedouin. Rising from her native marsh, she willingly drifts with the wind. Unlike the stegomyia she has no home and wants none.

The rarity with which infected stegomyiæ migrate has been indicated many times by the frequency with which houses so close to the infected dwelling as to be almost contiguous, and with coincident open windows, have escaped infection. It is further illustrated with regard to railroad cars by the fact that in each case in which we have been able to trace the manner of infection in a city or town, it has been found that the locality was infected by some person who, arriving there during the incubative period of the disease, subsequently developed the fever. In no instance has there been any legitimate evidence which would point to any other method of infection.

The idea prevailing among some people with regard to the traveling of the infected mosquito is ill founded. It unquestionably does travel, but only because in the incipiency of its life it has taken its habitat in a car instead of a house, or because, accidentally imprisoned in a box or drawer, it is carried, *nolens volens;* but rare, indeed, are such cases, and after studying yellow fever in Ocean Springs, in 1898, while doing postepidemic work there, the definite conclusion was reached that "yellow fever crossed the street here in a pair of shoes and in no other way."

Transportation has always been the most serious difficulty confronting us in yellow fever outbreaks, largely because of public timidity (on the outside). In 1905, because of popular clamor, we disinfected cars, both passenger and freight. We relayed passenger coaches and cut out Pullman traffic, so far as direct entry into the city was concerned. Most of this car disinfection and relaying was unnecessary, and in support of that view I wish to call attention to the fact that, having an abiding faith in the ideas stated, I purposely omitted any relay or disinfection of the Louisville and Nashville Railroad coaches out of New Orleans, going to the Alabama State line, where they were relayed upon the demand of Alabama. These coaches went from the city of New Orleans, traversing the entire width of eastern Louisiana and southern Mississippi, a distance of 116 miles, every day and every night, without any precautions whatever being taken until some weeks after the beginning of the outbreak, and then the windows were screened.

These cars were boarded at the Louisiana frontier by Mississippi national guardsmen who served as quarantine guards, and who traveled *in the cars* with the passengers from the western to the eastern border of the State of Mississippi and back again, day and night, in dry and in humid weather, for the whole period during which yellow fever existed in New Orleans. There were some score of them so exposed to any infection which might have existed in these coaches, but not a single one of these men so acting as train inspectors, nor any of the train crews, was taken sick with any kind of fever whatsoever, and I wish, in concluding this particular portion of my remarks, to accentuate the fact that these coaches traveled up and down Elysian Fields Street in the city of New Orleans, on both sides of which street the infection was rampant, as well as up and down the river front of the city, passing the original infected area where the infection was most prevalent, thus determining, at least to my mind, as strongly as circumstantial evidence may determine anything, that the *infected* stegomyia does not travel to any noticeable degree; that *it remains,* as nearly as it may, at the place *where it first tasted blood*, and will not voluntarily leave a house, much less cross a street. I have stated this before, but deem it of so much importance that it should be repeated and emphasized at every opportunity.

The case in which it cannot find food, water, and seclusion in the habitat it chooses at its birth, is rare indeed, and finding these, it needs no more.

While deadly dangerous when concealed, yellow fever is so easy of control, *if only* the medical profession and the *people will be frank and honest* with the health officers, that it seems a crime against humanity that we must needs quarantine such a disease. There is no more rationalism in quarantining yellow fever than there would be in quarantining typhoid. Indeed, there is less, because it may be stated as an absolute and invariable law, that a case of yellow fever known in the first two or three days of its existence, and to which proper measures can be applied, presents absolutely no menace to the community, nor even to the family resident in the house with it. Until, however, such laws are enacted and enforced as will make the concealment of a case of yellow fever, either through the complaisance of the family physician or the cowardice of the family, a crime and an absolute impossibility, there will continue to be more or less quarantine, probably more. Such laws are deemed by many people an interference with individual liberty and incompatible with the rights of American citizenship and other similar buncombe *ad nauseum.* The only other alternative, and a most excellent one, too, will be the passage and enforcement of laws insuring through the medium of paving, drainage, sewerage, and water supply, the proper sanitation of our cities, these being matters which offer so many other advantages in addition to the removal of yellow fever, as to make them the most imperative needs that confront those living in the zone.

We may rid the United States of yellow fever, but we will never rid it of its susceptibility to that disease until these four requirements are complied with, and the possession of these public utilities will also do away with many of the other "ills that flesh is heir to."

It is irrational to go on, year after year, fighting only the infected mosquito, when we can, with a little more trouble, destroy all mosquitoes once and for all. To put the matter plainly to the business man who is, after all, the court of last appeal, let us say to him: "Make an investment now in good health, and it will pay you enormous dividends in increased business, in reduced loss of time by yourself and your employees, and in that priceless boon which comes only to the man free from any taint of disease, the one only thing that makes our north superior to our south, the pure joy of living."

We of the south should do with purposeful minds what our northern cities have done, when aiming simply at comfort, they paved and drained and sewered their streets, and by purely accidental coincidence, obtained immunity from yellow fever.

There is no question but that drainage, sewerage, and paving will reduce the general average of humidity to a great extent, and in so reducing it, will also reduce the growth of the minor animal and vegetable life which we wish to minimize. Superadded to these, there should be an abundant and potable water supply, eliminating, absolutely, any other source of water, the cistern and rain barrel of the Gulf coast being, from a sanitary standpoint, the abomination of desolation. All these things may seem so essentially the primaries of sanitation that one is almost ashamed to recommend them, but they are, indeed, the most essential of all the moves which a municipality can make in the interest of its people's health from the standpoint of yellow fever prophylaxis, and until they are made, no community lying within what is known as infectible territory can hope for immunity.

The ideal condition at which we should aim, and this aim is not altogether utopian, is to so reduce humidity in cities within the radius of infectibility as to promote a condition of aridity so marked that, except in public parks alone, the growth of small animal and vegetable life must be cultivated artificially. Such aridity is ideal for any city, and more especially for those which have to deal with the risk of receiving yellow fever, and constitutes in itself the *ultima Thule* of yellow fever prophylaxis.

If I have injected into this discussion too much of my own work, I ask your pardon, for I have been thus guilty only because the whole story must be told if we would get at the remedy.

Surgeon General Wyman, in a recent address in Charleston, said: " The question: 'Am I my brother's keeper?' is more and more being answered Yes." Thank God, this is true, and I ask you who are specialists in the prevention of disease, to join hands in an effort to enlist the sympathy, not only of our own brethren, but of all mankind, to the end that we may so swell the volume of this responsive *Yes* that it shall resound throughout the whole earth. Let us endeavor to teach to all men, that no man has a right to so live his life that his carelessness and neglect of duty shall jeopardize the lives and happiness of innocent women and children, and to indelibly impress upon their consciences what they owe to their fellow men, until it shall be that he who so fails in his duty that his fault shall injure these innocent ones, shall be branded with the mark of Cain, and like his ancient prototype, be driven out by his fellows to be a vagabond and an outcast upon the earth.

ARE THERE VALID OBJECTIONS TO THE QUININ PROPHYLAXIS OF MALARIA?*

E. R. STITT.
Surgeon, U. S. Navy, Instructor in Tropical Medicine, U. S. Naval Medical School; Lecturer on Tropical Medicine, Jefferson Medical College.
WASHINGTON, D. C.

As with many other important questions the matter of quinin prophylaxis of malaria is largely one of compromise. Do the good results obtained under certain conditions hold generally, or are there exceptions—are there valid objections to its use other than the generally recognized one of preventing exact diagnosis?

In the first place, the ease of its application as compared with the better methods of mosquito destruction and screening, appeals to the sanitarian, especially in the tropics. It is just as easy to give quinin to a man in the tropics as it is in temperate climates, but when you consider the propositions of draining tropical swamps and shutting off circulation of air on a torrid night with fine wire gauze in the windows and closely woven mosquito nets around the bed, the question is decidedly different. In consequence, the tendency would be for the average man to despair of accomplishing anything in the way of mosquito destruction and screening and to seize eagerly on the inferior alternative, that of quinin prophylaxis.

Ronald Ross presents this matter concisely and to the point when he states that it is not a good policy to substitute a measure which does not exclude infection, but is merely extirpative in some cases, for positive prevention. From this it will be seen that unless it is clearly recognized that quinin prophylaxis may in some cases extirpate, but does not prevent, there might be a tendency to adopt this measure and neglect the two proper ones.

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* These statements are in substance the remarks made in the discussion of the paper of Prof. Thayer on Quinin Prophylaxis at the meeting of the American Society of Tropical Medicine, March 28, 1908.

As regards the relative merits of quinin prophylaxis and protection from mosquitoes Celli gives the following figures:

TREATMENT.	INFECTED.
Mosquito protection plus quinin prophylaxis.	1.75 per cent.
Mosquito protection alone.................	2.5 per cent.
Quinin prophylaxis alone..................	20. per cent.
No protection at all......................	33. per cent.

In 1895, I served as medical officer of the Ludlow Nicaraguan Canal Commission. It was my intention to recommend that members of the party take quinin as a prophylactic. On arriving at Greytown, I consulted with a physician who had been on the medical staff of the Nicaraguan Canal Company, and acting on his advice, I decided against quinin prophylaxis. He stated that their experience had been that quinin in doses that could be well borne had little effect in preventing the development of the disease; also, that it appeared to them that persons who had been taking quinin prophylactically were less amenable to its curative effects and that relapses had appeared to be more common in those following such practice than in those who only received the drug at the time of a malarial attack.

While in camp along the canal route we had a few cases of malaria. These were immediately treated with large doses of quinin, and without exception they responded promptly and satisfactorily to such treatment. The only member of the party who insisted on taking quinin prophylactically was Colonel Ludlow, the head of the commission, and strange to say, he was the only one who had malaria on the trip home.

To those who have thought of quinin prophylaxis as a true preventive the following instance is instructive:

On May 20, 1906, a battalion of marines, numbering 398, was organized at Philadelphia. Seventy-five per cent. of the force was made up of recent recruits from the Middle West. Leaving Philadelphia May 21, Colon was reached May 28. On June 4 the battalion was disembarked at Colon and stationed for a time at Camp Elliott, which is situated about 25 miles from Colon and which was comparatively free from mosquitoes. Later on, three companies were stationed at Camp Reed, five miles from Panama, at which place mosquitoes were numerous and troublesome.

On July 6, after a service of practically one month on the Isthmus, the marines returned to the ship (U. S. S. *Columbia*). During the month's encampment, 9 grains of quinin had been served out daily as a prophylactic. In addition, such measures as head-nets for those on night sentinel duty and inspection of mosquito nets about men sleeping in tents had been in force. There was very little malaria reported from these men while on the Isthmus.

The ship sailed from Colon on the night of July 7. On the first day out 20 cases of malaria were admitted to the sick list, the next day 53, and the third day 45. In consequence of what appeared to the medical officer to be universal infection among the men, ten grains daily of quinin were administered to every one as a prophylactic. Notwithstanding this almost curative dosage of quinin the condition of the men was such when the ship arrived at San Juan, July 13, that it was deemed necessary to get the men out of the tropics as several cases of a pernicious type and two of blackwater fever had appeared. Accordingly the ship sailed for Boston July 16.

Notwithstanding the prophylactic use of quinin, under military observation, for those who were not cinchonized, there were 215 acute malarial paroxysms among 298 men during the five days' trip from San Juan to Boston. About 100 men of the original 398 had been transferred to other ships and stations prior to the sailing of the *Columbia* for Boston. The character of the paroxysms was atypical—there was no frank chill. The men would feel fairly well until shortly before an attack—they would then complain of chilliness and weakness and either lie down or fall down in a heap on deck. Passed Assistant Surgeon Butler, U. S. N., states in a report that when the men arrived at Boston so many were anemic and weak that they were unfit to return to the tropics. Dr. Butler also noted the fact that these cases did not seem to respond at all satisfactorily to quinin even when given hypodermatically. Before the cases became so numerous blood examinations were made and the form of malaria was considered to be chiefly tertian. The clinical features, however, would indicate that there was estivo-autumnal infection in many of the cases.

In considering the experience of these marines who were given prophylactic, I might even say curative, doses of quinin during a period just exceeding a month, and when this was discontinued during the days of July 7, 8, 9 and 10, showed an extensive malarial morbidity, the question naturally presents itself as to the explanation of this. Furthermore, we must note the fact that resumption of quinin prophylaxis at this time in those not cinchonized appearently had little effect in checking the outbreak, and that when quinin was administered in curative doses, at times hypodermatically, it did not seem to control the infection as is usual. It is common experience that malaria responds readily and promptly to quinin properly administered. I can not but believe that malarial parasites may develop a resistance to quinin.

Browning, reporting recent work in Ehrlich's laboratory, states that when mice infected with trypanosomes were not given sufficient doses to destroy the flagellates, these protozoa developed a resistance to the therapeutic agent during the time their development was held in abeyance. A most startling discovery was, too, that these trypanosomes retained their chemo-resistance through numberless generations. After passage during a period of fourteen months through 144 mice these last generations of trypanosomes still retained their immunity to the exciting drug. Browning experimented with atoxyl, parafuchsin and trypan blue. Experiments with paramecium have also shown that these ciliates may develop marked resistance to agents primarily toxic to them.

I have seen actively motile amebæ in the stools of people undergoing quinin irrigation of the colon. I had generally considered that the explanation was that mucus had protected them from the toxic action of the quinin. May it not have been that these amebæ had developed resistance to quinin during the extended use of the remedy? Does it not seem that the malarial parasite may develop a resistance to a toxic influence which holds them in abeyance but does not destroy?

Another important consideration is that not only is the chief means of correct diagnosis, the finding of the parasite in the blood, made uncertain or useless, because it is common experience that even a single dose of quinin will drive the parasites from the peripheral circulation, but the frank manifestations of the malarial paroxysms are masked so that clinical diagnosis also is made difficult. When one considers the insidious and rather uncharacteristic paroxysms of estivo-autumnal fever this difficulty is more apparent. In this connection, the physician above referred to considered that as a result of failure to recognize malaria clinically institution of curative measures was delayed, and that as a result, the disease was more difficult to treat and relapses were more frequent.

Now at that time (1895) we did not know about parthenogenesis on the part of the macrogametes. Thanks to Schaudinn it would now seem that we have a scientific explanation. The sexual forms in estivo-autumnal fever do not develop for about ten days after the first paroxysm. In case we are giving quinin prophylactically we do not recognize the first attack and as time goes by the gametes develop. These being resistant to quinin, as shown by the experiments of Gualdi and Martirano, are not extirpated. Later on, the microgametocytes die out, leaving only the macrogametes. These by a parthenogenetic reproduction give rise to another non-sexual cycle and we have a relapse.

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THE LIFE AND WORK

- OF -

JAMES CARROLL*

By JOSEPH McFARLAND, M. D., Philadelphia, Penn.

To us whose lives are full of bustling activities, and who are still in the strife of endeavor, hoping for the crowning achievement that shall make our work worth while, it is a pleasure to spend a moment in affectionate admiration of one whose fight has been finished, whose work has ended, whose ambitions have been realized, who has entered upon his eternal rest and has become a treasured recollection to us all.

The American Society of Tropical Medicine mourns, to-day, the loss of James Carroll, one of the first elected honorary members, who made the first public address, at the first general meeting of the Society, in Huston Hall, at the University of Pennsylvania, Jan. 11, 1904, upon that work with which he was so closely identified, "The Etiology of Yellow Fever."

James Carroll was a remarkable man! He was such stuff as pioneers are made of—a composite of physical strength and endurance; mental keenness and sagacity; moral rectitude and courage; earnestness, gravity, sincerity and a pertinacity bordering on obstinacy. He was one of those rare men who make their own careers, not accepting those conditions into which accident brings them. He took life's burdens upon his shoulders without complaining and steadily forced his way beyond the common herd, by whom he was surrounded, to higher and nobler opportunities of which they never dreamed. And against what odds he fought the great battle of his life! A runaway boy without friends; an immigrant in an inhospitable country; an education abruptly ended in his fifteenth year; a private soldier in the United States Army with years of monotonous life in Western posts! These were his beginnings, yet see with what achievements his life ended! He was born in Woolwich, England, June 5, 1854, his parents being James Carroll and Harriet Chiverton, and attended Albion House Academy, Woolwich, until 1869, when he ran away from home, Dr. Kelly tells us, because of a disappointed boyish love, and came to America.

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*Memoir read at the Fifth Annual Meeting of the Society of Tropical Medicine, Baltimore, March 28, 1908.

He went first to Canada, where he spent the first years of his life in "roughing it" in the backwoods and doing hard work for little pay. Finding no prospects in Canada, he came to the United States, where he suffered great discouragements in finding a place for himself, so that in sheer desperation he, to use his own words, "drifted into the Army, enlisting January 9, 1874, before he was twenty years old. He served as a private [corporal and sargent?] in Company E, First Infantry, from January 9, 1874, to January 9, 1879, and as private [sargent and first sargent?] in Company C, Seventh Infantry, from January 22, 1879, until September 14, 1883—nine long years.

His service was mostly in the West, in Dakota, Montana and Minnesota. It was at Fort Snelling, Minn., that he met Hospital Steward Wm. Grant, who seems to have been the first to suggest to him the idea of securing advancement by becoming a hospital steward himself.

The idea appealed to Carroll's slumbering ambition, and embracing such opportunities as were kindly offered him by Grant and making good use of his time, he was able, after a year's study, to pass an excellent examination under Major W. C. Spencer, Medical Corps, U. S. A., and was appointed Hospital Steward, U S. A., September 15, 1883. He remained a hospital steward until May 21, 1898—15 years. In this new capacity his work continued in the West and his interest in medicine increased until he determined to study it as a profession. To accomplish this end he applied for a detail in order to study at St. Paul, Minn., but to his disappointment, the application was refused and his regular work continued until 1886, when he took a leave of absence, went to New York, and pursued a year's course at the Medical School of the University of the City of New York. His leave of absence having expired, he returned to the Department of the Platte, and resumed his work as hospital steward, continuing until 1889, when he was ordered for duty to Fort McHenry, Maryland.

He was not now alone, for in May, 1888, he had married Jennie M. Lucas, of Cleveland.

It may have been that the thought of other lives than his own to provide for, stimulated him to redoubled efforts, but in his new station he was happy in coming into close contact with Capt. C. B. Byrne, U. S. A., Post Surgeon, who sympathized with his aspirations and further stimulated his ambitions. He was now in a position where the continuance of his studies was possible, so he entered the University of Maryland, Baltimore, and was granted his degree in medicine in 1891. Immediately after this he took post-graduate courses in Pathology and Bacteriology at the Johns Hopkins Hospital, and became acquainted with that interesting family of which Prof. Welch speaks so fondly, composed of Councilman, Flexner, Lafleur, Thayer, Barker, Abbott, Nuttall and Reed.

Here seems to have been the beginning of an acquaintance that meant so much to Carroll, for it was through Reed, and with Reed, that his best work was done.

In 1893 he was detailed to the World's Fair at Chicago for special work in assisting Capt. L. A. LeGard, Medical Corps, U. S. A., and while there is said to have attracted the attention of Surgeon George M. Sternberg, because of his fitness for experimental work. At the close of the Fair he was transferred to the Army Medical Museum, Washington, D. C., where he remained associated with Reed. At this time the Army Medical School was established in Washington, Reed being made Professor of Pathology and Bacteriology, and Carroll Assistant Professor of the same subject. In 1895 Carroll was made a demonstrator in the Columbian (now George Washington) University, where Reed was Professor of Pathology and Bacteriology.

In 1897, at the instigation of Surgeon-General G. M. Sternberg, U. S. A., Reed and Carroll devoted themselves to the investigation of *Bacillus x* and *Bacillus icteroides,* Sanarelli. On May 22, 1898, Dr. Carroll was commissioned Contract Surgeon and First Lieutenant.

Early in 1900, yellow fever appeared among the American troops at Havana, and during the summer it became quite prevalent among the Americans and Spaniards in and about the city. In order to take advantage of this opportunity for continuing the study of the etiology of the disease, a board of medical officers was ordered to Havana for the purpose.

It was composed of Major Walter Reed, Surgeon, U. S. A.; Lieutenant James Carroll, Assistant Surgeon; Dr. Jesse W. Lazear, U. S. A., and Dr. Aristides Agramonte.

This is the commission that has become so famous, but of which only one, Dr. Agramonte, now survives. The commission reached Havana June 25, 1900, and within a day or two was organized and work begun.

It was unpromising business. The long and painstaking researches of Sternberg, and the mistake of Sanarelli, that grew every day more certain, were behind them and with them. But a new field of activity made possible by the great work of Manson and Ross upon malaria, and the suggestions of Finlay, opened before them, and after having satisfied themselves that Sanarelli and all the older workers were wrong, they turned to the insect hypothesis, greatly aided by Finlay, who had already fixed upon the mosquito now known as *Stegomyia fasciata,* as the probable host of the yellow fever parasite.

The work of the commission is too well known to need prolonged description, and Professor Welch has briefly synoptized it as follows: The commission proved,

1. The futility of Sanarelli's claims,
2. That the virus of yellow fever is in the blood,
3. That the virus is conveyed by the Stegomyia mosquito,
4. That the patient is a source for transmission only in the first three days of the disease,
5. That the virus must undergo an incubation period in the mosquito of twelve to fourteen days.

But we are reviewing the work of the commission and neglecting the story of the men who composed it. The most tragic part of their history was told by Carroll (*N. Y. Med. Journal,* February 6-13, 1904) in his address before this Society in the following words:

"Two separate lines of work now presented; one, the study of the bacterial flora of the intestine and anaerobic cultures from the blood and various organs; the other, the theory of the transmission of the disease by the mosquito, which had been advanced by Dr. Carlos Finlay in 1881. After due consideration it was decided to investigate the latter first. Then arose the question of the tremendous responsibility involved in the use of human beings for experimental purposes. It was concluded that the results themselves, if positive, would be sufficient justification of the undertaking. It was suggested that we subject ourselves to the same risk and this suggestion was accepted by Dr. Reed and Dr. Lazear. It became necessary for Dr. Reed to return to the United States and the work was begun by Dr. Lazear, who applied infected mosquitoes to a number of persons, himself included, without result. On the afternoon of July 27, 1900, I submitted myself to the bite of an infected mosquito applied by Dr. Lazear. The insect had been hatched and reared in the laboratory, had been caused to feed upon cases of yellow fever, two of them severe, and two mild. The first patient, a severe case, was bitten twelve days before; the second, third and fourth patients had been bitten six, four and two days previously, and were in character mild, severe and mild respectively. In writing to Dr. Reed that night of the incident, I remarked jokingly that if there was anything in the mosquito theory, I should have a good dose. And so it happened. After having slight premonitory symptoms for two days, I was taken sick on August 31, and on September 1 was carried to the yellow fever camp. My life was in the balance for three days, and my chart shows that on the fifth, sixth and seventh days my urine contained eight-tenths and nine-tenths of moist albumin. * * * On the day I was taken sick, August 31, 1900, Dr. Lazear applied the same mosquito, with three others, to another individual who suffered a comparatively mild attack and was well before I had left my bed. It so happened that I was the first person in whom the mosquito was proved to convey the disease.

"On the eighteenth of September, five days after I was permitted to leave my bed, Dr. Lazear was stricken, and died in convulsions just one week later, after several days of delirium with black vomit. Such is yellow fever.

"He was bitten by a stray mosquito while applying other insects to a patient in one of the city hospitals. He did not recognize it as a Stegomyia, and thought it was a Culex. It was permitted to take its fill and he attached no importance to the bite until after he was taken sick, when he related the incident to me. I shall never forget the expression of alarm in his eyes when I last saw him alive in the third or fourth day of his illness. The spasmodic contractions of his diaphragm indicated that black vomit was impending, and he fully appreciated their significance. The dreaded vomit soon appeared. I was too weak to see him again in that condition, and there was nothing that I could do to help him.

"Dr. Lazear left a wife and two young children, one of whom he had never seen."

Strange pathos runs through this story. It seems as if it was only after his own illness was over and the picture of the dying Dr. Lazear was before him, that he thought of what might have happened to his own wife and children had their positions been reversed.

In 1901 yellow fever broke out in Santiago de las Vegas, near Havana, and Carroll, who had been home on a leave of absence, again went to Cuba to continue the experimental study of the disease, reaching Havana August 11, 1901.

The enthusiastic interest he manifested in the progress made in the study of yellow fever and its prophylaxis, and the numerous papers that he wrote and addresses he delivered upon the subject, are well known to all here.

In 1902, Major Walter Reed, having died after a brief attack of appendicitis, Carroll was promoted to the position of Professor of Pathology and Bacteriology in his place. He continued to be a demonstrator in the Columbian (now George Washington) University until 1903, when he was promoted to be Associate Professor of Pathology and Bacteriology and appointed to succeed Reed as Pathologist to the University Hospital. In 1902 Carroll was also made Curator of the Army Medical Museum, and on October 27, was commissioned First Lieutenant and Assistant Surgeon in the regular Army.

In 1905 he was promoted to a full Professorship, which he retained until the time of his death. His professional work was always a source of interest and pleasure to him and of great profit to his students, who always showed him respect and esteem.

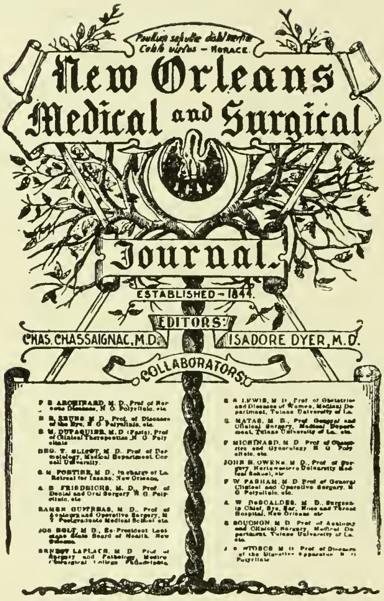
On May 27, 1907, Carroll had conferred upon him the degree of Doctor of Laws by the University of Nevada, in recognition of his scientific and humanitarian achievements. The work he did for his fellowmen was recognized in all countries by professional and laymen alike, yet the true recognition by his Government that should advance his rank appropriately to his service and increase his pay so that the support of his family of seven children could be carried on in comfort, came very late, and it was not until March 2, 1907, that through the influence of his many friends the United States Congress, by special act of legislation, ordered that he be advanced to the rank of Major and made a surgeon in the United States Army.

This distinction he was not long to enjoy. It is supposed by some of his friends that the attack of yellow fever was at the bottom of it all, but that may be sentiment rather than science. At all events, he fell into a lingering illness and died in Washington, September 16, 1907.

> "On the overworked soil
> Of this planet, enjoyment is sharpened by toil;
> And one seems, by the pain of ascending the height,
> To have conquered a claim to that wonderful sight.
>
> * * * * * * * * *
>
> Life relenting awards the good gift we would have,
> But as though by some strange imperfection in fate
> The good gift, when it comes, comes a moment too late."

So from obscure beginning may come magnificent endings! Through his English pluck and dogged perseverence, in spite of deficient education, expatriation, obscurity, isolation in military life, discouragement of all kinds—often in the face of poverty—James Carroll rose from the ranks to become one of the chief ornaments of the Army Medical Service, and one of the distinguished of his country.

Reprint from Vol. 61



,JULY 1908.

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PUERTO RICO AS A FIELD FOR RESEARCH IN TROPICAL MEDICINE.*

By Bailey K. Ashford, M. D., U. S. Army,
Washington, D. C.,
Honorary Member, Puerto Rico Anæmia Commission.

(*Under the Imprimatur of the Society of Tropical Medicine.*)

There are a few remarks which may be made concerning certain diseases classed as "tropical" to be found in the island of Puerto Rico which may, perhaps, interest the members of this society in a nearby and very inviting field of study.

I was for some years in a position to see a large number of current dispensary cases as well as to follow up some special cases in the hospital. Probably about 15,000 were thus personally seen, and fully 20,000 more were observed by colleagues working similarly in other parts of the island. These patients represent fairly the average clinic among the Puerto Rican laboring class, numerically large, as it constitutes the vast majority of the inhabitants of the country.

The society will, perhaps, be able to reach some conclusion concerning the value of Puerto Rico as a point of observation of some, at least, of the affections more or less foreign to our temperate zone.

Uncinariasis.—This is without doubt the most serious of all diseases in Puerto Rico, not only in point of numbers infected, but also in morbidity and mortality. It is not probable that in any other country it is really the leading affection. Its characteristics are well known, and no extended comment is necessary, save to remind you that it is

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*Read at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

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estimated that not far from 800,000 of its 1,000,000 of population harbored this parasite at the beginning of the American domination, and that from 5,000 to 7,000 died annually from its effects. Despite the approximate 150,000 to 175,000 persons treated by the Puerto Rico Anæmia Commission it still remains the distinguishing feature of Puerto Rican pathology, although now clearly understood and properly treated by practically all insular physicians. Although what has been elucidated by divers authors is common knowledge, there is no point at which profound anæmias and their effects can be better observed. Despite faithful attempts, no adequate explanation has yet been given of just how this anæmia is brought about. Many believe that it is a hæmolysis due to some product of the worm. This remains to be established by actual proof, and constitutes a scientific problem of great interest which can possibly be best worked out in this island.

Microfilaria nocturna.—This parasite is commonly encountered. Twelve per cent. of the second battalion of the Puerto Rican provisional regiment of infantry, stationed at Cayey, were found to be hosts of this parasite, and while nearly all the infected were apparently healthy men, their military medical histories displayed from time to time the capacity of this worm of evil. Whether this is a fair proportion of infected among the civil population is problematical. Suffice it to say that filariasis was frequently seen among our patients in Ponce, and chyluria, varicose groin glands, lymph scrotum, and other manifestations were constantly in evidence. Many were also found who suffered no symptoms. Cases of elephantiasis were by no means in proportion to the number of persons in whose blood microfilariæ were circulating.

One of the most interesting phases of the disease is the so called "erisipela" or erysipelas. This is a most common condition and seems to bear relation to filarial disease, in most instances, when affecting a lower extremity without other apparent cause. It was our custom to suspect such cases of filarial infection, and a search through the blood at night was often rewarded by finding the embryo worm. This "erisipela" is, of course, a complication with the usual sharp reaction of a lymphangeitis and is not at all fatal, as a rule, although I have seen it result in death; it is apt to end in elephantoid swellings of the limbs, if not in elephantiasis.

As will be seen from the remarks on this, as well as on the succeeding diseases, we were unable to give our time to a thorough study of these cases as uncinariasis was claiming most of our attention. There seems to be, however, a decided tendency for lymphangeitis of the lower extremity to recur again and again in filarial infectious. Can there be a reduced resistance to the invasion of the streptococcus and other pyogenic organisms? Our experience with the affection would seem to indicate it. It is needless to say that filariasis could be made a most absorbing, perhaps very profitable study in the interest of the large number of persons of all stations of life who are victims of the disease, for it is not alone confined to the poor. It is certainly much more common in the mosquito plagued coast regions than in the highlands of the interior, as may be imagined. and is not rarely confounded with malaria if the indispensable microscope is not called into service. This is especially true in those cases where the chill, high fever, and sweat are all the symptoms to be elicited, a not uncommon picture in filariasis.

Other varieties of microfilariæ were not observed, although from reports from neighboring islands it is not unreasonable to suppose that they are to be found.

Bilharziosis.—This is not at all infrequent, the first announcement of the disease in Puerto Rico having been made by Gonzalez Martinez to the Puerto Rican Medical Association early in 1904. Thirty cases were disclosed in the routine examination of the fæces of uncinaria patients by the commission, but these were not all that were seen by me. Others have made reports on bilharzia disease in the island, notably Gonzalez Martinez, of Mayaguez, who tells me that in 5 per cent. at least of the rural population of his district the eggs can be demonstrated in the fæces. Great interest attaches to this affection because of its exclusive limitation to the rectal mucous membrane. It is due, almost certainly, to the *Schistosoma mansoni* of recent description and is not *Schistosoma hæmatobium* as first believed.

Members of the commission repeatedly asserted their belief, based on the appearance of the ovum, that it was not identical with previously described schistosomata. Ova have never been found, to my knowledge. in the urine; the parasites were large, oval, and always provided with lateral spine. Apparently no symptoms are usually elicited, but that it can give rise to a serious affection is seen in the death of one of our patients, a child of twelve, in whom it was at least a contributory cause. During the long stay of this child in our field hospital, the infection was evidenced clinically by ulcerative proctitis and prolapsus recti, and the autopsy revealed many adult worms in the splenic and portal veins. The worms and tissues were unfortunately damaged in preservation by an assistant. Examination showed that the parasite was tuberculated.

The presence of the worm in Puerto Rico is believed by Stiles to constitute a serious menace to the island, a view borne out by the fact that cases of bilharziosis are apparently increasing in numbers. At one point, Mayaguez, the infection seems to be deeply rooted in endemic form. Opportunities for infection are never lacking among a large proportion of the population, as the people go barefoot, and there are no features of successful invasion to alarm a patient, until extensive changes are wrought and widespread dissemination of the ova has been accomplished.

As a rule, the effects are simply those of the local manifestation which, in aggravated form, with bloody and mucous stools, tenesmus, and pain, sorely tax the patience and strength of the host. No high eosinophilia has been observed by us. Indeed we question the eosinophilia of bilharziosis, but a fair test of many cases has not as yet been presented, as it is so very difficult to find a patient suffering from the disease, who is not at the same time the host of *Necator americanus,* a potent cause, as is well known, of a eosinophilia, even, for a considerable period after expulsion of all worms.

Ascaris lumbricoides.—This is a very common parasite of man in the island and is mentioned merely because it is so extremely frequent.

Oxyuris vermicularis is common. In connection with this worm, we stumbled upon what may be a valuable point in its treatment: As is known, the use every day or two of rectal enemata of salt and water, infusion of quassia, etc., for four to six weeks is recommended to effect a cure, as the female resides in the cæcum and only goes to the rectum after her eggs have matured, where, of course, she would be reached by the remedies above mentioned. In one of our cases 418 oxyurides were expelled, all the patient harbored, by two doses of betanaphthol of two grammes each; the second dose was administered one week after the first. This is a simpler and prompter method of treatment than the old one.

Strongyloides stercoralis is not infrequent.

Tricocephalus trichiuris is very common, but, while rebellious to anthelminthics, large numbers have been expelled by thymol and beta napththol, in spite of statements in medical literature, to the effect that they are insusceptible to its action. This worm may not usually cause anæmia, but we have seen cases in which it seemed to have done so. It occasions a moderate eosinophilia.

Trichinelliasis was never seen.

Filaria medinensis was not observed, and no evidence of its ever having been seen on the island can be obtained.

Cestodes are not at all frequent, and although *Hymenolepsis nana* was especially looked for it was not found.

Trematodes offer a fertile field for original work. Stiles reports in Osler's *Modern Medicine* upon a fasciola, sent him from one of the cases of the Anæmia Commission, and states that it is a new species. I have still another from another case found in Aibonito which is under consideration. *Paragonimus Westermanni* cannot be frequent if it exists in Puerto Rico. For several years I have searched for it, as have others, and as yet without result.

PROTOZOAN DISEASES.

Amœbic dysentery is not common, relatively speaking. Indirect testimony as to this statement may be offered in the well known fact that abscess of the liver is exceedingly rare. I saw but one case while in Puerto Rico. A few cases of pathogenic amœbæ were demonstrated in dysenteric stools.

Trypanosomiasis does not exist in the island.

Treponema pertenue must exist, although I have not seen it personally. There is clear and undisputed evidence of epidemic yaws, occurring in at least two districts some twenty years ago. It was typical from the description given by many who witnessed the cases, and it is not unreasonable to suppose that it will come to the fore again.

All care and diligence has failed to reveal kala azar and, while the suspicious of some workers must be respected, I have to record that all evidence is as yet utterly insufficient to warrant serious attention. Of the hæmosporidia only the *plasmodia* claim attention. Statements concerning malaria in Puerto Rico must be accepted with great reserve.

Positive evidence can be offered for certain valleys and for some coast districts. A remarkable feature of such foci, as were uncovered by the Puerto Rico Anæmia Commission, is the limitation of separate species to separate districts topographically distinct. For instance, while working in Aibonito with a district of about 8,500 population, about 4,000 came under our care for uncinariasis. It soon developed that in the large tobacco plantations of the valley of the river Plata, there was a focus where practically all cases were quartans, on the other side of us in another punch bowl valley, tertian prevailed, while from the sugar plantations of Aguirre nearly all cases which reached us were estivoautumnal. Thus within a few miles, in any one of three directions, we could enter three distinct foci, each populated by mosquitoes, bearing in one *Plasmodium vivax*, in another *Plasmodium malariæ*, and in a third *Plasmodium immaculatum.* This curious condition may, and probably does, obtain in other parts of the island, but the well known fact that there is, as in the early days of Greece, comparatively little migration of peasantry from one to another natural division of land will in part explain this curious distribution.

BACILLARY DISEASES.

Typhoid fever, while not a tropical disease, is apparently influenced by its tropical habitat. It is very fatal, and Manson's statement that it is twice as fatal in India among Europeans, as in the home country, can be applied not only to continentals but to Puerto Ricans in the island under consideration. This disease is gradually becoming a cause of alarm, and while it existed sporadically before, its rapid strides since our occupation are causing universal comment. Recently I am informed that the large town of Caguas has been visited by a severe epidemic. One such epidemic was observed in Cayey, a mountain town of the interior, and one in Coamo; later a similar one invaded the town of Aibonito, where the commission was working, but it did not reach serious proportions as in the other towns mentioned. Our observation led us to the conclusion that these outbreaks were often by contact infection.

A rich opportunity for the application of antityphoid vaccines is here presented, at a critical period, when such aid might be truly appreciated. It would be the only feasible way to put an end to what is already seemingly a serious condition, should the prophylactic value of the vaccine be established.

Bacillary dysentery.—At present the disease is not epidemic, nor was it during the existence of the Puerto Rico Anæmia Commission. We were informed that most severe epidemics are wont to fall upon the island at times. It seems to be the prevailing form of dysentery in Puerto Rico, and its character has been studied and reported upon by American investigators.

Plague has never been reported.

Cholera visited the island, during our own epidemic in this country.

Leprosy is not a common disease, but there is a colony at San Juan of perhaps fifty patients. I saw one case, suspected of this disease in Ponce by its health officer, in consultation with Dr. Joseph Goldberger, U. S. Public Health and Marine Hospital Service. This patient, whose nature was promptly revealed by scrapings from an incision into the anæsthetic lobe of the ear, was in hiding, and it is not improbable that there may be others of a similar nature, but such were not seen by any members of the commission. It may be of interest to know that all or nearly all cases are in native Puerto Ricans.

Yellow Fever.—Since the advent of the Americans, yellow fever, which, in the seven years preceding our arrival, gave an annual mortality of 161, has not been seen. *Stegomyia fasciata* are very abundant, however, and yet, in spite of this fact. there is much to confirm the general boast among the Puerto Ricans that the disease never really became endemic as in Cuba. Cases developed in certain towns open to commerce from that country and other infected posts, and usually in them only, but soon died out to be revived by fresh importations.

Glanders.—Several cases of glanders have been seen, and it has been not infrequent in horses, whose care is very poor.

Tetanus has been another serious question as a cause of infant mortality, but the responsibility for this state of affairs cannot be laid at the door of insular physicians. Dr. Francisco del Valle Atiles states, in an interesting thesis on the Puerto Rican peasant, in 1899: " . . . but of all diseases that an infant contracts shortly after birth, tetanus causes a higher mortality than any other. It can be said that the affection is endemic in Puerto Rico." I saw several true cases, and have heard of a large number of others, but the rate of 3.41 per cent. of the total mortality, given for the first seven months of our occupation of the island, and said to be about that for the ten years preceding, is certainly not due to the bacillus of tetanus. Many convulsions of infancy are wrongly attributed to it and so swell the reported mortality. It is, however, not at all uncommon even among adults.

Tuberculosis cannot be discussed here, but its ravages in towns are as great as its rarity among the people of the mountains.

OTHER DISEASES.

Beriberi is not a disease of Puerto Rico. It has been described in the island, but the reasonable doubt that uncinariasis was the true affection cannot be overcome, in the absence of examination of the fæces. The genuine danger of confounding certain cases of uncinariasis with beriberi is not to be lightly passed over. Of course, they are separated clinically in the vast majority of cases, but I have in mind now a case which would puzzle anyone without close study and, especially, in absence of a report on the examination of the fæces.

Sprue is not very rare; it occurs in foreigners to the soil and in some Puerto Ricans.

Malta Fevers.—Very careful search for Malta fever was made during several years but none was found.

Pellagra.—The writer has seen one case which appeared to be genuine pellagra.

Heat stroke is indeed rare, as Puerto Rico can hardly be considered a very hot country. This leads to the suggestion that the climatic effects of the tropics on our race be studied in this island. Even at high altitudes where it is cool and pleasant practically all of the time, "tropical neurasthenia" is in evidence. The nervous system certainly suffers in a manner not yet clearly worked out, where heat cannot be considered a potent factor.

I believe, that this climatic effect is not alone seen in strangers unaccustomed to this latitude. *Mal de pelea, ataques, mal de corazon* are popular names for a very common nervous manifestation which is really hysteria. This is the nearest approach to a true brain storm I have ever witnessed. It is frequently among some women of the poorer classes, and its name, "the fighting disease," is not belied, as anyone who has seen it can testify.

The subject is not exhausted, but nothing has been said about certain fevers which after some study do not fit into any classification, simply because they have probably not been sufficiently studied. There is room for some valuable original work, to clear up such as are still an enigma to many painstaking men in the island.

This rapid review of the tropical diseases of Puerto Rico will indicate the importance of this country as a centre for research. A few words may not be amiss concerning the facilities for such investigations.

In the past few years a great change has been noticed in the attitude of the people with regard to problems of hygiene. The eradication of smallpox and yellow fever, and the attack on the prevalent and dreaded anæmia, have had their effect in deepening respect for the advance of modern preventive medicine. There is truly a remarkable faith in all that tends to combat disease with scientific weapons, and this among the most lowly class. On the other hand physicians have been brought to a full realization of their power, when efficient means are taken to diagnosticate by methods which include judicious use of microscope and approved instruments of recent adoption, to treat causes, not effects, and to relegate to proper obscurity ancient and unreasonable drugs, which do little more than salve the conscience with empty promises of cure of symptoms. These physicians are generally graduates of foreign schools and their classical knowledge has been often acquired at some of the most famous European centres. Many of the recent graduates come equipped from excellent schools, both here and abroad, and have well supplemented the conservatism of practitioners, whose experience is of greatest value, by advanced ideas of medical thought and technique. The Puerto Rican Medical Association is a body of whom the island has reason to feel satisfied, and their tolerance and their desire for investigation of the problems affecting the health of their country are marked and worthy of the highest respect.

In such an island, isolated from extraneous influence, no better opportunity can present itself to demonstrate how modern conceptions of communicable disease can influence the health of a tropical country; and it is all the more of importance, when America can point to such satisfactory results in one of her new territorial acquisitions, in a group of islands, famous for years as points from which our knowledge of tropical pathology has been greatly enriched. We are, as it were, in competition with other powerful nations in the Antilles and we must "make good."

Scientific working parties may gradually develop a valuable centre for research. Puerto Rico offers special advantages for the undertaking of such a labor. It is a small island, densely populated with about 260 inhabitants to the square mile; 90 per cent. of its population can be classed as rural; it has good roads; and is within four or five days of New York by good steamers; it has a most beautiful and varied picture of mountain, valley, and level coast, and comfortable accommodations, and the ever attractive environment of new customs and people.

Laboratory facilities are to be had, but there is no large laboratory. The board of health has been very generous in the past, and aids scientific work in every possible manner. Besides this several physicians have at heavy personal cost developed small laboratories.

It is hoped that interest in this island may be aroused among the scientific men of our country, and, through this society, may make an effort to draw up some organized plan for coming into closer touch with the workers in this promising field for research.

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AN ACCOUNT OF DR. LOUIS–DANIEL BEAUPERTHUY,

A PIONEER IN YELLOW FEVER RESEARCH.*

BY ARISTIDES AGRAMONTE, M.D., OF HAVANA, CUBA.

In the year 1853, the Province of Cumaná, in the Republic of Venezuela, was no doubt properly considered by the enlightened nations of the world as one of the wildest and remotest regions of the earth; its closest foreign neighbor is the English island of Trinidad, which little imaginative effort may well establish as a fragment of the mainland, severed by seismic action during one of the numerous earthquakes which, even within the history of man, have carried terror and desolation throughout Venezuelan territory.

What could it interest the world then, that a virulent and extensive epidemic of yellow fever ravaged that obscure and benighted country in the year of which I write? Still, let us be thankful that because of the preservation of a few documents, the records of one who labored at that time in the same field as ourselves will not remain forever buried in the musty archives of those ancient institutions.

The subject of this biographic sketch was then forty-five years of age, having been born on the 25th of August, 1808, at Basse Terre, in the Island of Guadeloupe (French West Indies). After obtaining his degree of Doctor in Medicine from the Paris Faculty in 1837, he was appointed "Traveling Naturalist" for the Paris Museum of Natural History, returning in that capacity to the regions of the Orinoco, which he had evidently formerly visited.[1]

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* Read by title at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

He devoted most of his time to the microscopical investigation of disease, carefully studying, with the means then at hand, the urine, excreta, and secretions of his clients, with such patience and perseverance, that many ignorant though well-meaning persons were led to consider him a harmless " crank " on the subject of microscopy.

As early as 1838, he had evolved theories which ascribe a parastic origin to all the infectious diseases; at that date he presented to the Academy of Science (Paris) an essay, written in collaboration with his college-mate, M. Adel de Rosseville, in which he attributed the cause of putrefaction to the presence of animalcules in organic matter.

The fact that this man in the early forties traveled through the wilds of Venezuela, investigating with a microscope the tropical diseases which came under his observation, makes him sufficiently deserving, to my mind, of the high place which I claim for him among the pioneers in the research of tropical medicine.

Leprosy was a " hobby " which he rode to the moment of his death, which, unfortunately for the subsequent development of his cherished branches of medicine, occurred in September, 1871, while, as director of the Leper Hospital at Demerara (Georgetown), British Guiana, he was engaged upon the humanitarian enterprise of carrying out a method of treatment based upon his parasitic theory of the disease. In connection with this, it is interesting to note that, as published by his colleague, Dr. Bakewell, of Trinidad,[2] Dr. Beauperthuy's treatment of leprosy particularly enjoined repeated bathing and excessive alimentation, both of which means are to-day considered as absolutely necessary for the success of the many vaunted methods. As evidence of his undeniable intellectual foresight, I quote the second requisite which he describes in his method of treating leprosy. He says: "The patients should live in as healthy a locality as possible, and not in the neighborhood of marshes, etc. They are required to sleep under mosquito nets so as to prevent the sting of insects, which irritate and inflame the skin and perhaps propagate the disease."

It was because of the favorable report rendered by a special commissioner of the English Government, that Dr. Beauperthuy was appointed director of the Demerara Leper Hospital.

But that to which I desire mostly to call the attention of the society is the fact that Beauperthuy, as early as 1853, distinctly saw the rôle played by mosquitoes in the spread of malaria and yellow fever. With regard to yellow fever, the "striped-legged mosquito" attracted his attention, and he was the first one, to my knowledge, who called it the "domestic" species, a fact which to-day has been conclusively demonstrated.

A fortunate circumstance has placed in my hands the documents which testify to the truth of the above statements, one of them, the *Official Gazette* of Cumaná, of May 23, 1854,[3] a few paragraphs of which I shall quote here, is most valuable from an historical point of view, and I am happy for the opportunity afforded by the invitation of the American Society of Tropical Medicine, to present to our English-speaking colleagues these facts, as a late tribute, but a sincere one, to the memory of a fellow practitioner who, if not entirely unknown, has been absolutely overlooked or forgotten by our contemporaries.

He labored upon a sterile soil; the minds of men were not yet in a condition to accept views so iconoclastic of the old hypotheses, so contrary to the cult of miasms and other intangible and mysterious agencies of disease. And still, the preachings of the harmless "crank" attracted considerable attention among the political authorities of the surrounding country. We have seen that the Government of the Island of Trinidad appointed Dr. Bakewell to investigate Beauperthuy's treatment of leprosy, and the French Colonial Office detailed Dr. G. P. M. de Brassac, a navy surgeon of the first class, for the same purpose. The latter rendered a more complete report and entered upon an agreement with both Drs. Beauperthuy and Bakewell to try the method under discussion after becoming impressed with its merits in Dr. Beauperthuy's hands. Of Beauperthuy's ideas, it is needless to say that neither De Brassac nor Bakewell could understand a single word.

In his report, De Brassac says:[4]

"In combating the ideas of Dr. Beauperthuy, we shall not forget that we have known this excellent confrère, a veritable type of honorability and disinterestedness, always convinced and filled with good faith in his scientific errors. If instead of being a detached pioneer from the army of investigators, deprived voluntarily for more than thirty years of all aid granted by progressive science, Dr. Beauperthuy had remained in contact with the workers of his time, there is no doubt but that the passion for research which characterized him would have made him one of the most remarkable among them."

But Finlay had also been considered a harmless "crank" by many, until the United States Army Board demonstrated the mosquito's agency in the spread of yellow fever, notwithstanding the fact that he had something more tangible on which to base his claims, from the fact that Manson had already demonstrated what the insect could do in transmitting disease since 1879.[5]

Until Manson's demonstration of filaria transmission, since Beauperthuy's articles (1854–1870), no mention of insect agency in the propagation of disease can be found in medical literature. Finlay quickly followed, in 1881, with a paper read before the Havana Academy of Sciences,[6] expounding the fundamental principles of a theory which we know to-day as the modern doctrine of yellow fever transmission, and which, unknown to all then, was in fact a regenerated and strengthened revival of Beauperthuy's ideas, regenerated and strengthened by the accumulated knowledge of thirty years, which period had elapsed since its conception.

Man to man transmission of disease through the bites of insects was unknown before Manson's discovery; this was the point brought out by Finlay in his theory and in which it principally differed from Beauperthuy's at the time of which I write. On the other hand, Finlay and Beauperthuy had arrived at the same conclusion (the mosquito's rôle), by following a series of logical deductions, based exclusively upon the study of yellow fever epidemics. Neither one nor the other had knowledge, at the time of their respective publications, of any demonstrated evidence on which to base their claim, and, in fact, not until the publication of the investigations made by the United States Army Board was there any scientific proof that could be accepted by the medical world as incontrovertible.[7]

Two important points which were the subject of uncertain speculation were definitely settled only after the experiments of the Army Board above referred to (1900–1901); these were the period of incubation of the disease, and the time during which a patient may remain infective. Without both of these, to serve as a fulcrum, the mighty lever, even of such a master mind as Finlay's, could accomplish but little. In Beauperthuy's time, when native and foreigner alike were stricken by the dreaded scourge, even the positive knowledge of immunity was lacking.

Before going any further in studying the value of Beauperthuy's work, which can only be done by just comparison and a careful estimation of its merit and of its time, I may be permitted to quote a few paragraphs from his original contributions to the medical literature of those days.

In the above cited *Official Gazette,* he says:

" In the performance of the duties which I have undertaken [city physician during an epidemic of yellow fever, in Cumaná], I have applied the experience obtained during fourteen years of microscopic investigations made of changes in the blood and other fluids of the animal economy in the fevers of all types.

" These observations, made in the equinoctial and tropical regions, were of great aid to me in recognizing the causes of yellow fever and the appropriate means of combating this terrible disease. As to my work regarding the etiology of yellow fever, I shall abstain from making it public just at present. My investigations in this direction are part of an extensive work in which the results present facts, so new and so different from the accepted views, that I must not publish them without bringing to their support the most evident demonstrations. On the other hand, I am sending to the Academy at Paris a sealed letter which contains a résumé of the observations which I have collected up to date (1854), and the object of which is to insure against all events the propriety of my discoveries regarding the causes of fever in general."

It is my intention to obtain from the legal heirs of Dr. Beauperthuy authority to open the letter to which he refers; it is no doubt fraught with interesting data and thus we shall rescue one more document from undeserved obscurity.

Further on he says:

"The disease known as yellow-typhus, black-vomit, etc., is produced by the same causes which induce the intermittent fevers.

"Yellow fever cannot be considered as a contagious disease. The cause of this disease develops under climacteric conditions which allow it to spread at once or successively; these conditions are those which favor the development of mosquitoes (insectes tipulaires, maringoines, etc.)."

"The mosquitoes introduce into the skin their *sucker*, composed of a grooved sting or spur with two lateral saws; they instil into the skin a venomous fluid, which has the property of snake poisons. It softens the blood cells, produces a rupture of their tegumentary membranes, dissolves the parenchymatous portion and facilitates the solution of the coloring matter in the blood plasma. This dissolvent action seems to facilitate the flow of the blood through the capillary duct of the mosquito's 'sucker.'

"The agents of this infection (yellow fever) present great number of varieties, not all of them being equally harmful. The variety known as 'Zancudo bobo,' which has *white-striped legs*, is to a certain extent the *domestic species*. It is not the most common and its sting is comparatively less painful than that of the other species."

The following is an interesting statement, which shows Beauperthuy's power of observation and his good judgment:[8]

"It is not necessary to search very far in order to find why typhus icteroides is so common along the seacoast and so rare in the interior of the country and in localities little frequented by mosquitoes. In Basse Terre, capital of one of the West Indies, it has been observed that the epidemics of yellow fever do not extend their harmful influences as far as the town of Matouba, situated barely three miles from said city. It must be admitted that this distance is entirely too short to preserve, by itself, the town of Mantouba against the supposed noxious effluvia exhaled by the coast and which the winds, when blowing from the east, would transport within a few minutes; on the other hand, this distance from the sea, that is, from the locality inhabited by mosquitoes, is more than sufficient to preserve against their action and the serious inconveniences which they produce."

Beauperthuy thought that mosquitoes obtained the yellow fever poison from the putrefying organic matter in the stagnant waters in which they breed; this grave error is quite excusable when we consider the meager medical attainments of his day.

Speaking of malaria fever, he says:

"The intermittent fevers are severe in proportion with the abundance of mosquitoes, and these fevers disappear or lose much of their intensity in the woods which, on account of their altitude, contain but few of these insects.

"The marshy emanations are reputed as more energetic during the night than in the rest of the day. These are the hours in which mosquitoes are most active.

" To protect themselves against the fevers, the Indians employ certain preservatives, and those who inhabit the unhealthy valleys place burning coals (a brazier) at the entrance of their huts. This method is very effective for barring mosquitoes.

" Of all means employed to protect themselves from the action of mosquito bites, the most efficient is that followed by some Indians, which consists in rubbing the skin with oleaginous substances."

Upon acclimatization, he says:

" Perhaps we ought to look upon acclimatization only as an inoculation.. It is not that the febrile virus introduced under the skin of man preserves him from the fevers, but that it diminishes the harmful action of these diseases and makes them lose a great part of their gravity. It acts as the variola inoculation, although the latter does not always preserve from pustulous infections. This analogy is still more evident in yellow fever, which generally affects the individual only once."

Further on we find:

" Contagious diseases are transmitted by inoculation. A certain period must elapse between the action of an infecting cause and the start of a visible lesion."

" The expression ' winged serpents,' used by Herodotus, is well applicable to the tipulary insects and the action of their bites upon the human economy."

The collection of Beauperthuy's papers, published under the title of ' Travaux Scientific,' contains a great deal of matter which is just as absurd in our judgment to-day as his mosquito theory must have been to his contemporaries; there is a good quantity of chaff and irrelevant material in his writings; numerous pages are filled with obscure meaning, but now and then, as through a rift in heavy and accumulating clouds, a ray of light, clear and distinct, shines forth to give us a glimpse of the truth which he could see, no doubt, in spite of the bigotry and ignorance of the times.

Finally, allow me to quote a paragraph from another article:

"The attachment to old ideas is always protected by indifference and indolence. The worship of errors is otherwise as passionate as that of truth. It is necessary to remove from medicine those erroneous explanations which disfigure it. Truth can be established but very slowly; it cannot come forth except after a struggle, after having destroyed the errors which occupied it's place. It was only after thirty years of debate that Harvey could demonstrate the circulation of the blood, a thing in which the proofs are easily established. The products of the imagination shining with greater splendor than the real facts are often substituted for the truth. Fantastic glares! Physicians, in the impossibility of discovering the causes of a great number of diseases, imagine an invisible power, occult, intangible to our senses and beyond our means of investigation. The routinary spirit of many physicians is content with this vague appreciation of the sources of most diseases and makes no effort to penetrate into the real causes of epidemics and of contagious diseases which are still unknown. From this point of view, science requires a complete renovation."

I consider the evidence here presented quite sufficient on which to base a claim for recognition of this investigator, lost in the devious by-ways of tropical America; it seems to me that it also serves to prove that, like all great truths which have been brought forth in medicine, since the earliest history of the art, the modern doctrine which explains the propagation of yellow fever had a prolonged and distressing evolution extending over a period of half a century.

If we eliminate the questionable credit which has been ascribed to Nott, who in 1848 vaguely suggested the possibility of insect transmission for both malaria and yellow fever, we find that in 1854 Beauperthuy speaks plainly of mosquitoes spreading epidemics of yellow fever and that he, thinking several species were responsible, fixes upon the domestic habits of the striped-legged variety; then, in 1881, Finlay defends the hypothetic mosquito transmission, introduces the feature of man to man infection and presents the striped-legged and the Culex pipiens (C. cubensis) as the probable vehicles of infection; later he retains only the striped-legged mosquito as the propagator of the disease. Then in 1900–1901, the experiments of the United States Army Board definitely settle the question of mosquito transmission; they establish the exact maximum limit of incubation in man, the minimum in the mosquito, the infective period of yellow fever cases and fixes the guilt upon the single species Stegomyia calopus. Subsequent investigators have only corrobated the findings of this board.

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THE PREVENTION OF TROPICAL ABSCESS OF THE LIVER BY THE EARLY DIAGNOSIS AND TREATMENT OF THE PRESUPPURATIVE STAGE OF AMEBIC HEPATITIS.*

LEONARD ROGERS, M.D.
CALCUTTA, INDIA.

During the last seven years I have enjoyed most exceptional opportunities for studying tropical abscess of the liver in Calcutta, and have now arrived at the conclusion that the disease can and should be prevented altogether in the great majority of cases. The following are briefly the steps by which I have reached this position:

In 1902[1] I published a paper on tropical, or amebic, abscess of the liver and its relationship to amebic dysentery, in which I gave tables to show that I had found living amebas in scrapings from the walls of 35 out of 37 consecutive liver abscesses, the two negative results being in those not examined until twelve or more days after the abscess had been opened and drained. Further, two-thirds of the abscesses, when first opened, were sterile as regards the presence of bacteria. Kruse and Pasquale had previously found amebas in only 6 out of 15 cases examined. I also showed that when both a clinical history and a postmortem record were available, in over 90 per cent. of the cases dysentery was found to be associated with the liver abscess, and in 95 per cent. of these there was evidence that the dysentery had preceded the formation of the abscess, while it was always, in my experience, of the amebic variety. I, therefore, concluded that the large tropical abscesses (as opposed to those due to suppuration in the portal veins or in the bile ducts) were always due to the *Amœba dysenterica,* and secondary to amebic dysentery, although the latter might often be of a latent nature, giving rise to no typical dysenteric symptoms during life, but revealing itself in the form of a few amebic ulcers found postmortem, usually high up the large bowel in the cecum or ascending colon.

In a second paper[2] in 1903 I gave an account of amebic dysentery in India and discussed the formation of amebic abscess of the liver. In 1905[3] I dealt with the value of leucocytosis in the early diagnosis of amebic abscess and pointed out that, although occasionally an attack of acute hepatitis with leucocytosis may clear up without suppuration occurring, yet, if such cases are followed up, sooner or later an abscess of the liver nearly always forms. I also narrated a case of acute hepatitis with leucocytosis, which cleared up under large doses of ipecacuanha.

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* Read at the fifth annual meeting of the American Society of Tropical Medicine, held at Baltimore, March 28, 1908.

1. Brit. Med. Jour., Sept. 20, 1902.

2. Brit. Med. Jour., June 6, 1903.

3. Brit. Med. Jour., 1905, ii, 1291.

In 1906[4] I published two cases of amebic abscess of the liver successfully treated by aspiration and injection of the soluble bi-hydrochlorid of quinin, without drainage, having found that the amebas in thick liver abscess pus could readily be killed by that drug in a strength of from 1 in 100 to 1 in 500, a method which has since proved effective in other hands, especially in early deep-seated abscesses, although it fails in many more advanced cases.

While on the lookout for the early stages of the disease for this line of treatment, I met a number of cases of fever with leucocytosis and symptoms of acute hepatitis, in some of which aspiration failed to reveal any abscess. They yielded, however, very rapidly to full doses of ipecac, thus showing that the increase of the leucocytes takes place before actual suppuration has taken place and sometimes many days earlier. Last year (1907) I published[5] a series of such cases which were rapidly cut short in the presuppurative stage by the ipecac treatment, which may be briefly summarized as follows: Fifteen cases were met in the Calcutta European General Hospital during twelve months. In only three was there a clear history of dysentery or symptoms of it while in the hospital, and they lost their fever and hepatitis after two to four days' ipecac treatment, although they had previously suffered from fever for 15, 34 and 41 days, respectively, and one had been aspirated for liver abscess with a negative result. In three more cases of acute hepatitis without dysentery not treated by ipecac, the fever subsided only after 34 to 49 days. In five similar cases treated with ipecac the fever subsided in 1 to 6 days, although it had previously persisted for 13 to 50 days, one patient having been aspirated for liver abscess with a negative result. Lastly, there were three cases of fever with no signs of either dysentery

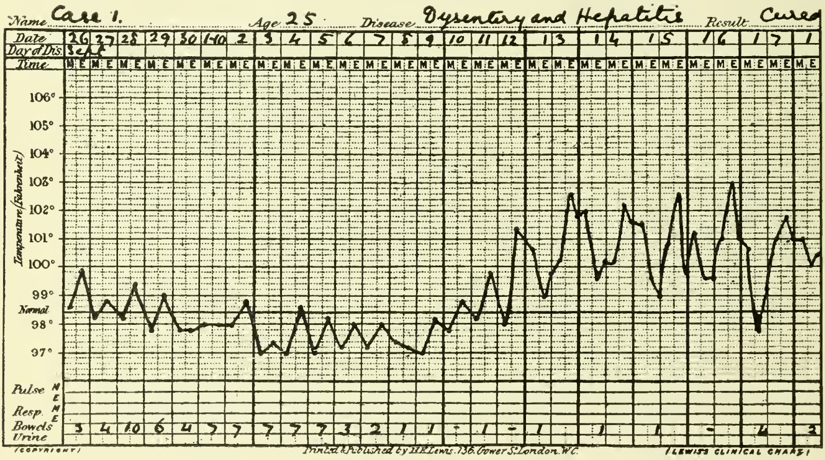

Chart 1—Case 1.

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[4] Brit. Med. Jour., June 16, 1906, i.

[5] Practitioner, Lond., 1907, lxxviii, 776; Tropical Fevers in the Tropics (Oxford Medical Publications).

or hepatitis, other than very slight painless enlargement of the liver, but with leucocytosis of the same type as in the other cases, namely, without very marked increase of the polynuclears (usually from 70 to 80 per cent.). They had suffered from fever for 35, 45 and 53 days, respectively, but it ceased in two to fifteen days under ipecac treatment. This is the class of case in which a large, deeply-seated, fibrous-walled abscess of the liver forms very insidiously with irregular intermittent fever, commonly treated as malarial, but with no very obvious signs of hepatitis until a very late stage. Two of the above fifteen cases relapsed and returned to the hospital 4 and 7 months later, respectively, each with an amebic abscess of the liver.

When dysentery is present and complicated by hepatitis, ipecac is advised by Sir Patrick Manson and other authorities, but at the time the above paper was published I was unable to find any recent writer who recommended large doses of ipecac for hepatitis when not accompanied by dysentery, although several of the older Indian authors, especially McClean and Norman Chevers, strongly urged its use in such cases also. The considerations which led me regularly to adopt this treatment were: First, finding dysentery associated with 90 per cent. of tropical abscesses of the liver, and, second, the fact above mentioned that in many patients dying of liver abscess, without history or symptoms of dysentery, amebic ulcers are found postmortem in the upper part of the large bowel. I, therefore, regarded hepatitis accompanied by leucocytosis as an indication of the presence of latent amebic ulceration of the large bowel, which indicated large doses of ipecac for its cure. The results of this treatment, both those mentioned above and subsequent ones, have been so successful that during the last two years no instance of liver abscess developing while the patient was in the European General Hospital, Calcutta, has occurred, although a few patients have been admitted with an abscess already formed. On the other hand, a number of very acute hepatitis

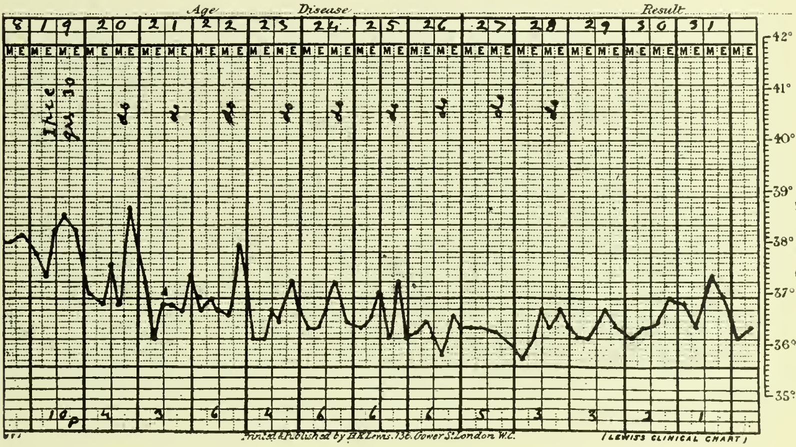

Chart 1—Case 1—Continued.

cases have cleared up under ipecac after an abscess had been suspected, and in five instances also sought for in vain with an aspirating needle.

REPORTS OF CASES.

The following three examples, which have occurred within the last two months, will serve to illustrate the value of this method of early diagnosis and treatment:

VERY ACUTE HEPATITIS CLOSELY FOLLOWING ON DYSENTERY RAPIDLY CURED BY IPECAC.

CASE 1.—A European, male, aged 25, was admitted for dysentery of six weeks' duration, passing about six stools daily containing blood and mucus, without pain or straining. He was treated with a castor oil mixture and creolin enemas, and the blood and mucus disappeared from the stools after ten days. Seven days later (September 11) he began to have pain in the hepatic region and in the right shoulder, and his temperature, which had previously been slightly subnormal, began to rise (Chart 1). The liver dulness was not increased, extending from the sixth rib to the costal margin. The pain continued to be severe, and on the 13th the breath sounds were noted to be weak at the base of the right lung. Morphia was being given for the pain, and ten grains of quinin three times a day for the fever. On the 15th there was profuse sweating, while the liver dulness now extended up to the fifth rib. Five leeches applied over the liver relieved the pain somewhat. On the 16th the right lower chest was observed to be moving less than the left, and on the 18th *x*-rays showed that the diaphragm on the right side was quite motionless, while there appeared to be a slight shadow in the right lobe of the liver. Abscess of the liver was, therefore, diagnosed. As, however, there had been recent dysentery, which had not been treated with full doses of ipecac, the physician in charge of the patient (who had over twenty years' Indian experience) agreed to use the ipecac treatment for a short time before operating on the liver abscess, the existence of which he did not doubt. Thirty grains of the drug were given daily from the 19th to the 27th, with the result that the temperature steadily fell, as shown in Chart 1, and the signs of acute hepatitis simultaneously subsided. On the 20th the pain over the liver and the sweating had both diminished and he slept better. By the 21st the pain had ceased over the liver, although it continued in a slight degree in the right shoulder for another day. On the 23d the temperature was normal and there was no pain or sweating, and all suspicion of liver abscess had disappeared. The patient was kept in the hospital up to the 22d of November,

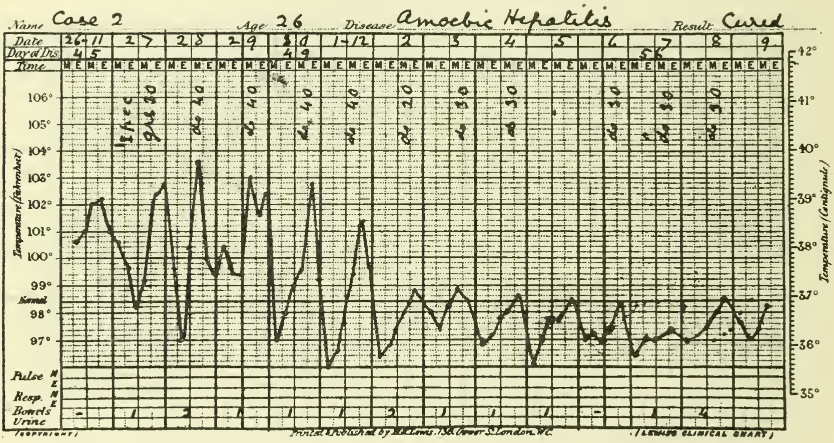

Chart 2—Case 2.

but had no more signs of dysentery or hepatitis and gained weight steadily. There was no shadow of doubt in the minds of all who watched this patient that the ipecac treatment averted suppuration in the liver.

DYSENTERY FOLLOWED BY HEPATITIS WITH TEMPORARY IMPROVEMENT, VERY ACUTE HEPATITIS TWO AND ONE-HALF MONTHS LATER SUCCESSFULLY TREATED WITH IPECAC.

CASE 2.—European, male, aged 26, admitted Aug. 20, 1907, with a history of dysentery eight months before, followed after three weeks by pain in the epigastrium. On admission he had slight enlargement of the liver with pain over it. Stools loose, but no blood or mucus; intermittent fever rising to 101 or 102 F. in the evenings. The diaphragm moved well, and there was only slight increase of the leucocytes, with but 65 per cent. of polynuclears. The symptoms of hepatitis subsided in three weeks under salines and quinin, and he left the hospital apparently well. He returned two and a half months later (November 26), having had fever every evening for the previous month and a half, with rigor at times and sharp pain over the liver on and off. His bowels had been constipated. He was now weak and thin. There was slight bulging, without marked tenderness, in the hepatic region. The breath sounds at the right base were diminished, with a decrease of vocal fremitus and vocal resonance. The liver dulness extended from the fifth space to three inches below the costal margin in the nipple line. No edema was present, and the spleen was not enlarged. Under *x*-rays the right half of the diaphragm was found to be two inches higher than the left and scarcely moved even with deep respiration, but there was no shadow. A blood count showed 3,570,000 red corpuscles, 15,000 white; ratio of white to red, 1 to 236; polynuclears, 77 per cent.; lymphocytes, 13 per cent.; large mononuclears, 9 per cent., and eosinophiles, 1 per cent. On account of the acuteness of the symptoms and the fulness in the hepatic region, liver abscess was suspected, but it was determined to try the ipecac treatment before operating, so 30 grains were given on the evening of the 27th and 40 grains on the following four evenings. On the 28th and 29th the hepatic pain was distinctly less, and the patient could turn over on his right side, which he could not do before. On the 30th there was no pain or tenderness over the liver. On December 2 his temperature remained normal for the first time, and a steady convalescence ensued, the liver receding until it was only just felt beneath the costal margin. The ipecac was continued in 30-grain doses at increasing intervals up to Jan. 5, 1908, in order to guard against the possibility of a relapse, and he left the hospital apparently quite well on January 5. The rapid lessening of the pain, followed by the de-

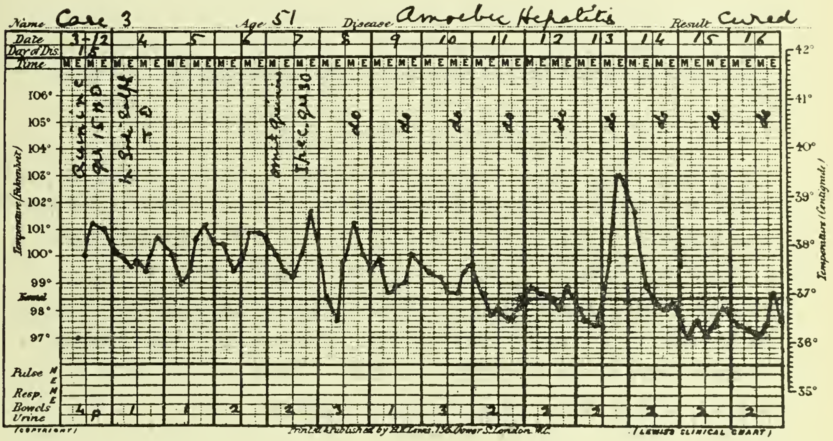

Chart 3—Case 3.

cline of the fever and enlargement of the liver under the ipecac, was most striking in this case, and indicated that this treatment saved the patient from suppuration in the liver.

HEPATITIS WITHOUT HISTORY OR SYMPTOMS OF DYSENTERY RAPIDLY SUBSIDING UNDER THE IPECAC TREATMENT.

CASE 3.—European, male, aged 51, admitted on Dec. 3, 1907, for fever. He had been ill for two weeks with fever and pain in the right hyphochondrium, with nausea and loss of appetite. No rigors, but feels chilly at times and sweats at night. Bowels constipated. The liver extends one inch below the costal margin and was very tender. Other organs normal. A blood count on the 11th showed 4,670,000 red corpuscles, 12,875 white; ratio of white to red, 1 to 363; polynuclears, 81 per cent.; lymphocytes, 12 per cent.; large mononuclears, 6, and eosinophiles, 1 per cent. Ipecacuanha was commenced on December 7, 30 grains being given each evening. Two days later the temperature began to fall and reached normal on the 11th, after which there was only one rise on the 13th, accompanied by a rigor, being possibly malarial in origin. On the 17th the liver had become reduced in size, being only just felt below the ribs, and the patient left the hospital apparently quite well on December 22 (Chart 3). This is an example of the less acute form of hepatitis, which drifts insidiously on into suppuration after weeks of intermittent fever. It is only one step further to the class already mentioned, in which there is no pain or tenderness over the liver, and the presence of leucocytosis alone raises a suspicion of the true nature of the case, which is confirmed by the chronic fever yielding rapidly to large doses of ipecac.

METHODS OF GIVING IPECAC.

In giving large doses of ipecac in amebic dysentery and hepatitis, precautions have to be taken to avoid vomiting, especially if it is possible that an abscess of the liver has already formed. The usual method is to give either tincture of opium or chloral hydrate some twenty minutes before the freshly made pills or bolus of ipecac, no food or drink being given for several hours before and after the dose, which is best administered once a day in the evening. Recently I have had the drug put up in quantities of five grains in keratinised capsules, which are not dissolved until they reach the small intestines. This has worked very well, no antecedent sedative being required. Dr. F. B. Grubbs, of the United States Army, has recently informed me that the same desirable effect is obtained by coating ipecac pills with melted salol, but I have not yet had an opportunity of trying it. From 30 to 60 grain doses of the drug have been used, but the smaller quantity appears to be efficient. It should be continued for at least two weeks at increasing intervals, as two of my earlier cases, in which the ipecac was discontinued as soon as the temperature fell, relapsed some months later, presumably owing to the latent amebic ulcers not having been completely cured.

DURATION OF THE PRESUPPURATIVE STAGE OF AMEBIC HEPATITIS.

There remains to be considered a very important question: What is the usual duration of the presuppurative stage of amebic hepatitis, during which the ipecac treatment will avert the formation of an abscess of the liver? An examination of my records of the last seven years has furnished the following data on this point: Out of 53 native patients admitted to the hospital with liver abscess, often bulging through the thoracic or abdominal wall, 51 per cent. gave a history of over two months' illness, and 38 per cent. more between one and two months; 9 per cent. from two weeks to a month, and only one case, or 2 per cent., had been suffering for less than two weeks. Among 26 cases in Europeans there had been fever of hepatitis for over one month in 50 per cent., for from two weeks to a month in 34.6 per cent., and of less than two weeks in only 15.4 per cent, the times being 9, 9, 11 and 13 days, respectively, in these four cases. It is clear from these figures that in the vast majority of instances there is ample time for the diagnosis by blood examinations. etc., and for the ipecac treatment being carried out during the presuppurative stage of acute amebic hepatitis. Very rarely multiple abscesses may develop within a few days with extreme acuteness, but even here the only chance of saving the patient is in the immediate ipecac treatment.

My experience of this treatment leads me to believe that it is not too much to say that over 90 per cent. of amebic abscesses of the liver can and ought to be prevented by the methods described in this and in previous communications, and thus one of the greatest scourges of some tropical countries may be conquered by the prompt use of a simple medicinal treatment, based on the correct conception of the true pathology of the disease derived from prolonged combined microscopic and clinical observation.

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HISTORY OF A CASE OF MALARIAL FEVER, ALGID FORM, CHOLERAIC TYPE.*

BY R. H. VON ESDORF, M.D.,

Passed Assistant Surgeon Public Health and Marine-Hospital Service, New Orleans Quarantine Station, Quarantine, La.

During the past year a number of cases of fever were removed from vessels coming from tropical ports to the Quarantine Hospital, New Orleans Quarantine Station, for observation and diagnosis.

There were 69 cases of malarial fever, 11 cases of typhoid and a number due to other causes, such as pneumonia, rheumatism, diseases of the digestive tract, etc., treated at this hospital. There were also a number of cases of malarial fever and typhoid fever which were diagnosed and allowed to proceed on the vessel to New Orleans of which no clinical record was kept.

The majority of cases of malarial fever had an estivo-autumnal infection. Stained preparations of blood were used in making a search for the parasite in all cases; sometimes a differential leucocyte count was also made; pigment was looked for in leucocytes. These laboratory aids, together with clinical course, were used in differential diagnosis.

Nearly all cases had points of interest, but one in particular occurred which was not diagnosed until after autopsy. This case I will cite; the history is as follows:

On Aug. 16, 1907, the Mexican steamship

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* Read by title at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

Puebla arrived at this station at 2.05 P.M. from Tampico where the vessel had been during the past thirty days. While the vessel was being fumigated the usual inspection of the crew was begun at 3 P.M. The temperature of each member was taken and recorded at this inspection and then a careful visual inspection of each man made. The pulse was felt, eyes examined, etc.

At this inspection I stopped to speak and examine more minutely than customary one individual who was a German. I spoke to him in his own language. I had noticed that he had a muddy complexion and was cachetic in appearance. He appeared to be dull or stupid, and was slow in making answer to my questions. His temperature was 36.6° C. Pulse normal. He appeared to be otherwise well and had nothing to complain of. Being a German, and not speaking Spanish, he did not converse with the other members of the crew, but spoke to them by making signs. I ascertained from the captain that the man had, on the voyage, complained of pain in his abdomen, which was attributed to seasickness; that his temperature had been taken with a clinical thermometer and found to be 37.4° C. He had been on watch at his regular turn during the voyage from Tampico except the one day he was thought to be seasick. The man signed on the vessel July 28, 1907, at Tampico.

On Aug. 17, 1907, this same man, A. F., took coffee at 5.30 A.M. with the other members of the crew and appeared to be about the same as usual during the morning. Nothing unusual was noted.

At 11 A.M. he was asked if he would not go to breakfast. He had no desire to eat, and it was thought that he wished to rest, as he had not slept during the night on account of the mosquitoes. None of the crew except the officers slept during the night for the same reason.

At 12.30 P.M. he was seen walking up and down the deck, when the captain asked what the trouble was, and he reported himself sick, pointing to his abdomen.

At 2 P.M. he was seen lying in a hammock which was stretched on the deck under an awning, where he was apparently sleeping.

At 4.30 P.M. the chief engineer reported to the captain that the man appeared to be suffering and was very sick. The captain at once went forward and noticed that there was considerable change in the man's appearance and he at once ordered a boat to be lowered to bring the man ashore, when he observed the Quarantine launch coming and he decided to await my arrival.

I was aboard in a few minutes and the captain reported the illness at once. I went forward and saw the man, whom I at once recognized as the same one I had carefully questioned the day before, suffering with what appeared to be abdominal pains. I spoke to him and ascertained that he had continuous pains, which were cramplike; that he had had diarrhea and had gone to the toilet frequently during the past few hours; that he had not vomited. His extremities were cold, skin a little moist, pulse small and irregular, face pinched, eyes glaring, pupils dilated, lips pale, tongue pale and dry, and apparently in collapse.

I ordered and gave him an ounce of brandy and repeated this in ten minutes while the launch had gone ashore to get a stretcher which I had ordered, that he might be carried to the hospital. I had also noticed that the man had evidently had involuntary stools, as his trousers were stained. There was also a stain on his legs, which was of bloody mucus and greenish yellow. The cramps came and went about every fifteen to thirty seconds. Abdomen was flat and became rigid during the pain. Legs were drawn up during pain and relaxed at intervals when pain subsided. He was apparently exhausted.

Upon inquiry from other members of the crew I ascertained that he had been seen going into the closet at intervals of from one to three minutes. One man noticed him enter and leave six times; each time he left he would take a drink of water and return to the closet. The crew went about their work, and the German, who could not speak their language, did not intimate his condition to any of the men. He had not complained except the one time at 12.30 P.M.

The man was carefully removed and taken to the launch, where he was placed on a stretcher, and while steaming toward shore fell into a syncope and died just before landing.

The illness had been so sudden in its onset that no diagnosis was ventured until a post mortem could be made.

Autopsy. — One half hour after death. Five thirty-five P.M. Aug. 17, 1907.

Adult male, 5 ft. 5 in. in height. Hair sandy. Skin dark muddy hue. Eyes blue white; pupils partly dilated. Lips blue, tongue pale, no corrosions about the mouth, hypostatic congestion beginning in spots. Hands those of a laborer. Rigor mortis setting in.

Incision made in median line. Section dry and bloodless. The intestinal tract was the first examined. No evidence of poisoning presented.

The peritoneal cavity had an excess of clear serous fluid, but no evidence of peritonitis could be seen. No intestinal obstruction.

The small intestine was flat, the large intestine flat and the same size as the small intestine and to all appearances absolutely empty. Peritoneal surface of the intestines smooth and glistening.

It was then noticed that the omentum was nearly black in color, that the entire mesentery was also black, but no macroscopic evidence of thrombi, emboli or hemorrhage presented. Large vessels of mesentery intact.

The large intestine was then opened its entire length. It was absolutely devoid of fecal matter and gas and contained nothing but bile-stained serous fluid. The mucous surface had some scattered bloody mucus adherent to it. No gas in any part of it.

Ileum, jejunum and duodenum were opened; the same character of fluid was present as found in the colon; no ulcers; no change in the mucous membrane could be noticed. There was no gas in any part of the intestinal tract except in some places the fluid was frothy; no particles of solid matter nor fecal matter were seen; absolutely no odor could be detected on opening these organs. Mesenteric glands not enlarged, apparently normal.

Stomach contained about 1 pint of bile-stained yellow fluid, the same as was found in the intestinal tract. There was an odor of brandy perceptible. The mucous membrane was completely intact, no corrosions or ulcers, but one thing was noticeable which was not seen in the intestines; this was, that the mucous membrane was black in appearance throughout. Esophagus, abdominal end, apparently normal.

The liver was enlarged, weight 6 lb., firm and of dark slate color. On section little blood exuded, color the same as the external surface. Gall bladder distended with bile.

Spleen.— This was found to be large, weight 1½ lb., soft and dark in appearance. On section my first remark was, " It cuts like a clot of blood." It was found to be very friable and the cut surface was diffluent. Pancreas appeared normal. Lungs appeared normal.

Heart and pericardium. — Pericardium contained more than the normal amount of fluid. No evidence of pericarditis was present. Heart was soft and flabby, distended with blood, in asystole. A blood slide was taken from the heart blood; also a smear from the spleen. No edema. No evidence of renal disease. Nothing else was noted from the normal.

I was satisfied that the case was not one of acute poisoning or a suicide, but felt sure that the cause must be toxic. The man had not eaten anything to give him ptomaine poisoning so far as I could ascertain, so this cause could be excluded.

My first concern was, that I must be satisfied that I was not dealing with a quarantinable disease. Choleraic symptoms had predominated, but finding a fluid in the intestines which was not rice water in character, but apparently serous and bile stained, settled the question negatively for cholera. I was puzzled for a short time. Then I thought that the spleen was certainly malarial and was indicative of the probable illness, and this conformed with the first impression that the man was a malarial cachetic. I then made the provisional diagnosis of acute malarial toxemia of the algid form, choleraic type.

I left the examination of my slides for the next morning. These were stained with Wright's polychrome methylene blue. The blood slide was a poor one, but I found a clear area under low power where the blood cells seemed to be flat and separate. I then examined this under high power and was struck with the presence of so much black pigment free and in white cells. The red blood cells showed a small ring form of the malarial parasite with its thin blue ring and red chromatin spots. Nearly every cell was so infected with one or two to three such young parasites. This was conclusive that it was malaria. The slide made from the spleen was then examined and found to be full of pigmented bodies. I reasoned then that the appearance of the mucous membrane must have been due to pigment which blocked the capillaries; that the appearance of the mesentery and omentum was due to the same condition.

Sections made of the liver and spleen tissues, stained with hemalum and eosin, showed them to be full of hemozoin in granules and large and small masses.

I regret that a blood count was not made, as there was unquestionably a marked, at least relative, leucocytosis. A differential leucocyte count from two slides gave the following results:

Small mononuclear leucocytes,	1,743	
,, ,, ,, pigmented,	25	68.8%
Large mononuclear leucocytes,	288	
,, ,, ,, pigmented,	173	17.9%
Polymorphonuclear leucocytes,	269	
,, ,, pigmented,	68	13.1%
Eosinophiles,	4	.15%
Total,	2,570	

I can at least safely report a marked leucocytosis, as may be judged from the above count.

I suppose that treatment would have availed had the case been recognized earlier, but certainly not at the time the case was seen by me. Had the man presented even a slight elevation of temperature I would surely have made a blood examination at the time of my first inspection, and would have given him quinine even if the examination had proven negative, as I would have been guided by the malarial aspect presented.

I frankly admit that I did not diagnose or even suspect the true character of the disease until after the autopsy was made by me.

The history just given was submitted to the surgeon-general's office and a copy also sent to Surgeon M. J. Rosenau, Director of the Hygienic Laboratory. Dr. Rosenau in his letter to me says, "He surely had an accesso pernicioso." "Don't you suppose, however, that he might have been sick on the trip and that when you saw him he was suffering with the stupor due to clogging of the capillaries of the brain with malarial pigment and parasites?"

I believe this was probable.

To recapitulate. We had a case presenting: Illness of about six hours; symptoms of cholera; no fever; syncope and death.

Post mortem: Enlarged liver and spleen; discolored mucous membrane of stomach; discolored mesentery and omentum; sections of liver and spleen showed hemozoin in large and small masses; young small ring form of malarial parasites in red blood cells and some free in the blood; hemozoin in white blood cells chiefly mononuclears; lymphocytosis; free hemozoin in blood.

Reprinted from the MEDICAL RECORD, June 20, 1908.

CLINICAL CHARTS OF A CASE OF QUARTAN MALARIAL FEVER OBSERVED IN WEST AFRICA, WITH COMMENTARY.*

By F. CREIGHTON WELLMAN, M.D.,

BENGUELLA, WEST AFRICA.

INFECTION with the quartan malarial parasite is a comparatively rare condition in the part of Portuguese West Africa studied by the writer, namely southern Angola. In a series of 531 cases of infection studied by me[1] only fourteen cases showed this form of parasite, all the remaining fevers being due to invasion by malignant parasites. Benign tertian has not yet been seen. In view of the local rarity of quartan fever the writer, some time ago, decided to observe carefully the progress of a case of the disease. The greater part of the working hours of one week were given up to the gathering of the data exhibited in the following charts. The case was observed for its intrinsic interest, the writer having no thesis to defend nor other aim than the first-hand acquisition of clinical facts regarding the disease as it exists in this district, from whence it had never been reported prior to a communication from the author of this paper[2]. Notes from a medical diary and a few additional observations in the form of comments have been added to the charts.

Case Notes.—Milemba, twenty-five years old, male, a Bantu, had always lived at a point about 1,300 meters above sea level. Being partially crippled he had never been into the more unhealthy lowlands along the coast. He had suffered from slight fevers from time to time all his life but never had severe ones. Was taken sick two days before I saw him.

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*Read by title at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

[1] Atti della Societá per gli Studi della Malaria, Rome, 1907, pp. 29-58. 1 plate and 8 figures in text.

[2] Journal of Tropical Medicine, London, November 1, 1905, p. 319.

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When first seen the patient had a temperature of 103° F., pulse, 90; respiration, 28. The spleen was slightly enlarged and somewhat tender. The blood was slightly alkaline by Haycraft-Williamson's method and showed in benzol-chloroform mixture a specific gravity of about 1.055. As to its tonicity I only tested it by adding to it a 0.41 per cent salt solution which, however, gave no hemolysis. On microscopical examination, quartan gametes and a few small ring forms were seen, with one or two pigmented leucocytes. The erythrocytes were normal in shape and size and no nucleated red cells were seen. Counted by the Thoma-Zeiss method, the number of erythrocytes was 4,700,000; leucocytes 7,000, hemoglobin index by Gower 90. A differential leucocyte count gave the following percentages (about 500 counted): Lymphocytes, 33 per cent.; large mononuclears, 29 per cent.; polymorphonuclears, 27 per cent.; eosinophiles, 11 per cent. The patient was a plump, well made man weighing 154 pounds (English) and was 5 feet 8¾ inches tall. He walked with a limp, having lost the toes of his right foot.

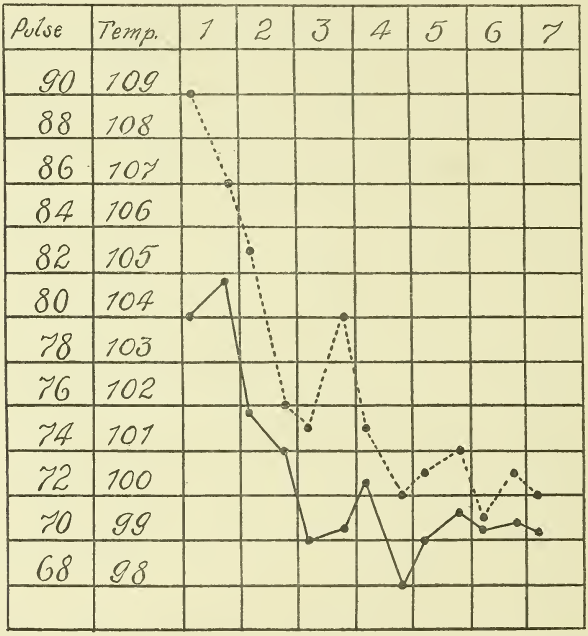

Chart I.—Pulse and Temperature. The continuous line indicates the temperature as taken in the mouth.

Method of Study.—The following routine was followed throughout the observation. The temperature and pulse were taken twice daily, always at the same hour. The blood for microscopical examination was also taken twice a day as near as possible at the same hour each day. Two wet and two dry specimens were always made, the latter to be stained, one by Leishman's modification of Romanowsky and the other with hematoxylin and eosin. The number of red and white cells was counted on the Thoma-Zeiss hemocytometer. On two occasions the result was compared with readings on the hematokrit. The hemoglobin index was taken by Gower's hemoglobinometer. The differential leucocyte counts were made on slides stained by hematoxylin and eosin. The patient was weighed daily at the same hour, and the amount of urine passed was measured and the number and size of stools noted. All the fluids ingested by the patient were measured and the solids weighed. No medicines were given or allowed.

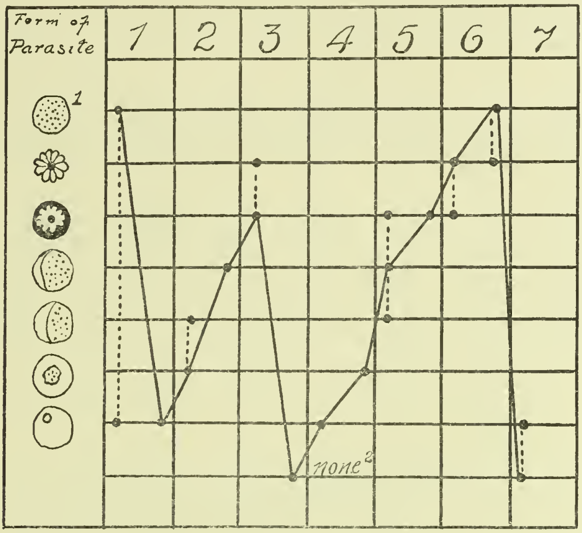

CHART 2.—The Shapes of the Parasite Seen in the Blood at Different Times. The line representing the parasites refers to the developmental stages observed and not to the abundance of parasites in the blood. The forms of the parasite are shown at the left of the chart. [1]Gamete. [2]A few parasites were found on the evening of the third day in a thick film preparation.

Commentary on Chart I.—The temperature curve is very different from the classical quartan type. In other cases which I have seen in West Africa there was even slighter rise of temperature (not over 100° F.) and in one or two cases no elevation of temperature at all, although the developmental cycle of the parasite went on steadily and regularly in the blood. In the case before us there was not, I believe, a double infection. Of course this is hard to pronounce upon categorically, but the small ring forms (with which alone malignant parasites could be confounded) did not seem to be in excess of their usual proportion and did not appear at the time one would expect them in a tertian. Close search was also made for crescents and other signs of double infection. Rest in bed seemed to be the chief factor in calming down the clinical manifestations. The accelerated pulse and respiration slowed down as the temperature fell. After the first day the patient was quite comfortable and by the third day wanted to get up.

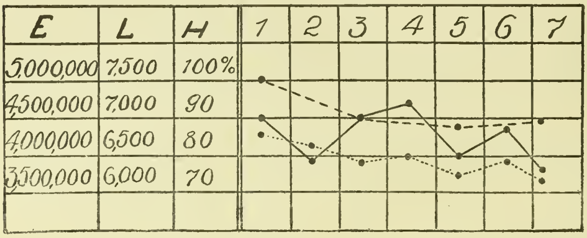

Chart 3.—Comparative Numbers of Erythrocytes and Leucocytes, with Hemoglobin Index. The continuous line indicates the erythrocytes (E), the broken line the leucocytes (L), and the dotted line the hemoglobin percentage (H).

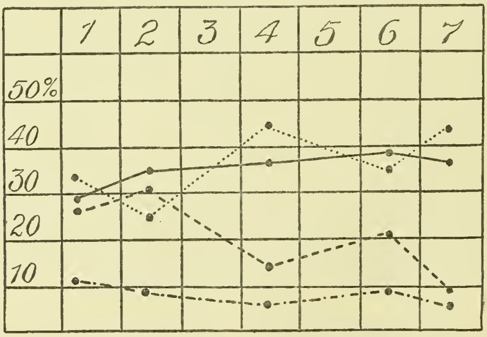

Chart 4.—Results of Differential Leucocyte Counts. The dotted line indicates the percentage of lymphocytes; the continuous line that of large mononuclears; the broken line that of polymorphonuclears, and the dotted-broken line that of the eosinophiles. About 500 were counted each time. N. B. The "transitionals" were always counted with the polymorphonuclears.

Commentary on Chart 2.—It will be seen on comparing this chart with Chart 1, that the sporulation of the parasite went on without the slightest relation to the temperature and pulse. This chart does not show all the forms seen in the blood at any one time, but only the form which preponderated during each stage. I have tried with dotted lines, however, to indicate other forms which were numerous and to connect them with the chief form. For instance on the morning of the first day segmenting forms could be seen with the gametes as well as small ring forms and even a few larger ones. The time and sequence of the development stages of the parasite in this case were not so regular and typical as I have seen in cases in Europe.

Commentary on Chart 3.—This chart shows that both the absolute and comparative numbers of the red and white corpuscles remained practically unchanged throughout the period. It will be seen, however, by comparing the erythrocyte count and hemoglobin index that the oxygen-carrying power of the blood was rather lowered, probably as a result both of hemolysis and corpuscular deficiency. The leucocytes, already scant, as is often the case in malaria, fell a little. The further behavior of the leucocytes is shown in the next chart.

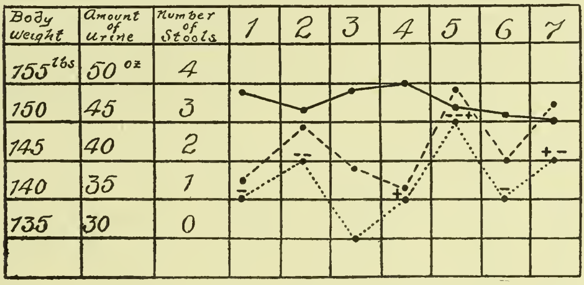

CHART 5.—The Changes in Body Weight Compared with the Amount of Urine and the Number of Stools Passed During the Period. The continuous line indicates the body weight in English pounds; the broken line the number of English ounces of urine passed in twenty-four hours; the dotted line the number of stools in twenty-four hours (+ denotes a large stool; — a small stool).

Commentary on Chart 4.—The differential leucocyte count shows no marked phagocytic tactics. The increased percentage of large mononuclears is characteristic of a malarious country. The eosinophiles and large mononuclears appear to be the most constant, but food taking and other factors may very well account for the polymorphonuclear and lymphocytic variation. The number of eosinophiles is not unusual for natives of this country (where some sort of helminthiasis is almost universal). I have frequently seen as large a proportion in individuals apparently enjoying the best of health. Entozoal infection probably accounts for such conditions.

Commentary on Chart 5.—The body weight decreased but slightly during the attack. The smaller amount of urine passed during the first part of the attack is probably to be explained by the fact that the patient perspired more freely at that period than later. The urine became much lighter in color during the last three days of the observation. This chart should be compared with the following one.

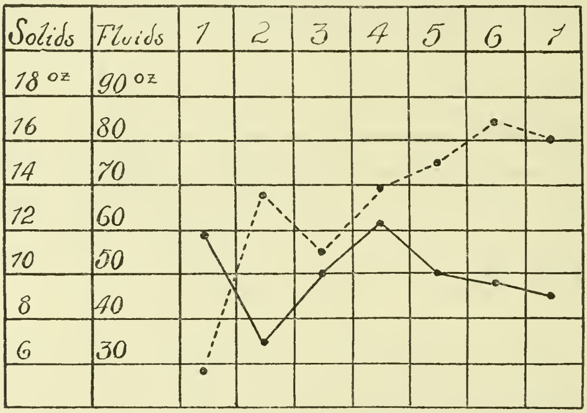

CHART 6.—Comparative Amounts of Fluids and Solids Ingested During Each Twenty-four Hours of the Disease. The continuous line indicates the fluids in English ounces; the broken line the solids in ounces.

Commentary on Chart 6.—The appetite increased as the patient grew better. The ingestion of liquids was the greatest on the first and fourth days of observation, and lowest on the second. The food and drink as a rule consisted of a fermented native gruel called "Ochisangua," made of meal from maize (*Zea mais* L.) and cassava (*Manihotutilissima* Pohl) mixed with water and the juice of a root called "Ombundi" (*Eriosema muxiria* Baker). For the last three days of the observation some solid food was taken with this.

General Commentary.—The foregoing is an attempt to add to our knowledge of the behavior of the quartan malarial parasite in tropical climates. Some points of interest brought out are: (*a*) the effect of warmth and rest in lowering the temperature and pulse rate; (*b*) the somewhat irregular sporulation of the parasite;(*c*) the relatively little damage done to the blood; (*d*) the constancy of the relative proportions of the leucocytes; (*e*) the small loss of body weight, and the general well-being of the patient without medical treatment; (*f*) the morphological identity of the parasite with the quartan parasite of other countries.

In conclusion, I may say that while the quartan fever of West Africa is the same as that of temperate climates, yet the mischief done is far less. It should be mentioned here that the patient declared himself perfectly well before he was discharged, and on his discharge immediately began manual labor. It would seem that in negroes of tropical climates who have acquired sufficient immunity to be generally fever-free in districts swarming with malignant malaria, such a benign disease as quartan (which in Europe gives rise to fevers quite severe enough) is a comparatively negligible factor.

Reprinted from the MEDICAL RECORD, July 25, 1908.

THE PATHOGENESIS OF PERNICIOUS MALARIA.*

By WILLIAM H. DEADERICK, M.D.,

MARIANNA, ARKANSAS.

PERNICIOUS malaria is almost as varied in pathogenesis as it is in its manifestations. Not only are its several forms associated with unlike conditions, but for the explanation of some the presence of several different factors is necessary. Thus, comatose malaria may be associated with at least two different forms of the parasite; the peripheral blood may show very great numbers of these parasites or they may be scanty; in the brain they may be found in hordes, even to the occlusion of small vessels, or they may be entirely absent.

As may be inferred no one etiological element can account for all cases, even of the same type. Probably the only essentially common factor is the presence of the malarial parasite, the manifestations of which run the gamut from the mildest intermittent to the profoundest cachexia, from the most artfully masked to the deadliest pernicious.

Until comparatively recently it was believed that infections with the so-called benign organisms never gave rise to pernicious symptoms. Celli[1] states that the tertian and quartan parasites never cause pernicious fevers. Marchiafava and Bignami[2] say that there is no instance on record of a malignant fever following tertian and quartan infections and that no autopsy has ever been made in connection with a malignant spring tertian or quartan. Mannaberg[3], Van der Scheer[4], and Maurer[5] believe that only the estivo-autumnal parasites have a rôle in the production of the pernicious fevers. Thayer, in his "Lectures on the Malarial Fevers," says that he never heard of a pernicious paroxysm occurring in tertian or quartan infections with the exception of the case of French.[6]

*Read by title at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

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While the vast majority of cases of pernicious malaria are due to infection with the tropical parasites it cannot now be maintained that tertian and quartan infections are not occasionally accompanied with perniciousness. Craig[7] says that any of the malarial parasites may cause pernicious infections leading to death. Crespin[8] informs us that it is not rare to find on examination tertian and quartan parasites in these cases. Billet[9] found the large tertian in six of forty cases of typhoid pernicious. Ziemann[10] observed a case of pernicious malaria due to the benign tertian. Thiroux[11] found this parasite in a case of convulsive pernicious in a mulatto infant. Ewing[12] in sixty-four cases of the cerebral type of pernicious, found the large tertian parasite alone in five. French[6] reports a case of comatose malaria in a man, age twenty-one, whose blood harbored the tertian parasite. Hunt[13] observed a case of common tertian complicated by alarming hematemesis in a boy aged eleven. McElroy[14] had a case of comatose pernicious due to tertian infection in a negro male, aged thirty. Ficucci[15] records a case with a pernicious meningo-cerebellar syndrome due to tertian parasites. Fenner[16] gives the history of a case of the comatose type in an adult; the blood examination showed crescents and large tertian forms.

Craig[7] makes the assertion that quartan infections are more apt to become pernicious than tertian. The writer, however, agrees with Davidson,[17] who says that pernicious symptoms occur more rarely in connection with quartan infections than with simple tertian. The reasons for this are probably the relative rarity of quartan fever and the more even distribution of parasites throughout the circulation, there being slight tendency to form accumulations.

It is not yet known with certainty which variety of the estivo-autumnal parasite gives rise most frequently to perniciousness. Marchiafava and Bignami[2] and Mannaberg[3] hold that the tertian estivo-autumnal infections are the most dangerous, only a few cases showing the quotidian. Craig,[18] however, found the quotidian parasite most often in cases infected in Cuba and in the Philippines. This was also the experience of Wright,[19] in British Malaya, who found the pigmented quotidian parasite most frequently associated with the cerebral and gastrointestinal types of pernicious malaria.

The part played by the crescents in the pathogenesis of pernicious paroxysms is worthy of brief consideration. Marchiafava and Bignami,[20] Celli,[1] Mannaberg,[3] A. Plehn,[21] Koch,[22] Manson,[23] Thayer,[24] and others believe that this form of the organism is nonpyrogenic. Ewing,[25] however, holds with Laveran that it is by no means certain that the formation and development of the crescents are entirely innocuous to the patient. Ewing doubtless in part bases this opinion on the finding of crescents alone in thirty-three of sixty-four cases of cerebral pernicious.[12] Whether the blood examined in these cases was peripheral or visceral is not stated, but as only three were fatal it may fairly be assumed that in most instances, at least, it was peripheral. That the crescentic form of the parasite has an intimate relation to the production of the pernicious fevers is improbable for the following reasons: First, crescents alone may be found in the peripheral blood and intense localizations of active forms be present in the brain or other viscera. The number of parasites in the superficial circulation is not a reliable guide to the severity of the attack. In eleven of Ewing's sixty-four cerebral cases no parasites were fully identified, and in many of his thirty-three cases in which crescents alone were found the search was successful only after one and two hours. Secondly, crescents are rarely if ever present in the parasitic localizations and thrombi frequently observed in pernicious cases.

Of the pathogenetic factors which excite perniciousness the following are to be regarded as the most important and approximately of relatively equal importance: 1. An excessive number of parasites. 2. Localizations of parasites. 3. Toxins. 4. Individual predisposition and external etiological influences.

Number of parasites. Golgi's law, that the number of parasites determines the severity of the attack, has been generally accepted. Cases in which the parasites are in very great numbers in the peripheral blood are usually accompanied by coma.

We have no means of estimating even approxmately the total number of malarial parasites in the body of a malarial patient as the distribution of the former varies within the widest limits. They may be numerous in the peripheral and visceral circulation generally; they may be scanty or absent in the peripheral circulation and numerous in most of the viscera; or they may exist in moderate numbers or be absent except in certain areas where they may be intensively localized. That the parasites are abundant, either absolutely in the body as a whole, or relatively in certain areas, probably holds good in a great majority of the cases, though, as Celli[1] states, we cannot always attribute perniciousness to the large number of parasitic forms. Marchiafava and Bignami[20] call attention to certain grave cases of comatose, convulsive, delirious or mixed pernicious in which from beginning to end and even at autopsy very few parasites are found. Mannaberg[3] says: "From the general impression which I have obtained, naturally only from the peripheral blood, the number in malignant fevers is perhaps larger, yet the difference scarcely seems so decided as to make this factor alone responsible for the perniciousness."

As applied to the number of parasites in the peripheral blood Golgi's rule is applicable only in a very general sense. Ziemann[26] states that the number of parasites in the peripheral blood is not always in direct relation to the severity of the attack. Crespin[27] acknowledges that he had difficulty in finding the parasites, which were always scanty in these cases. He gives the details of a case in which there were neither parasites nor pigment in the peripheral blood but they were numerous in the vessels of certain viscera. This writer quotes Nocht as saying "in pernicious attacks the hematozoa are not found in the peripheral blood but only in the viscera." Moore[28] says "I have often seen cases where the symptoms in no wise seemed commensurate with the number of parasites observed in the specimen of blood." According to Kendall[29] there may be only a few parasites in the peripheral circulation or it may even be impossible to find them. Mannaberg[3] states that it sometimes happens that the peripheral blood is very poor in parasites. Marchiafava and Bignami[20] note the fact that the contradiction found so often during life between the number of the parasites and the gravity of the disease disappears when an autopsy allows of an examination of all the organs. Craig[18] asserts that "the number of parasites found in the peripheral blood is not always a criterion as to the perniciousness as one of the most rapidly fatal cases I have ever observed showed but few parasites in the peripheral blood." To quote Barker[30]: "In the estivo-autumnal infections the number of organisms circulating in the peripheral parts affords, as a rule, very insufficient data upon which to base an idea of the severity of the infection." Thayer[24] says that there may be very few parasites in the peripheral circulation. He mentions a fatal case of the comatose variety showing no active parasites in the peripheral blood and only a very few ovoids and crescents after a careful search of the blood obtained by puncture of the spleen. Marchoux[31] reported three cases of pernicious malaria in which the parasites were very scanty in the peripheral circulation. Zeri[32] records four cases of pernicious fever in all of which the parasites were few in number. Bloombergh and Coffin[33] treated a case ending fatally in which no parasites could be found until forty-eight hours after onset notwithstanding repeated examinations. In seven cases in which Fenner[16] examined the blood, no parasites were found in five. Ewing's[12] eleven cases of the comatose form in which no parasites were fully identified have been mentioned. I have observed one case of severe comatose malaria in a boy aged 12 in whose peripheral blood the parasites were scanty.

On the other hand the superficial circulation may be teeming with parasites while the patient experiences only a mild attack. Thus A. Plehn[34] gives the histories of two cases in which the symptoms were slight though the peripheral blood showed as many as thirty-five and forty-six tropical parasites respectively to each field of the microscope.

It is highly probable that an enormous number of parasites, equably distributed, depends for its power to elicit pernicious symptoms upon the increased quantity of toxin elaborated.

Localization of Parasites.—Accumulations of parasites in the brain were first described by Planer (1854) and by Frerichs (1861), those in the liver by Guarnieri (1867). More recently the minute observations of Marchiafava and Bignami, Dock, Barker, and Ewing have taught us that pernicious malaria in many of its varied manifestations is dependent on these localizations in one or more of a multiplicity of localities. Localizations in the brain have been found associated with a wide variety of cerebral symptoms; in the mucosa of the alimentary tract with gastrointestinal symptoms and typical algid attacks; in the heart with cardiac symptoms; in the medulla with bulbar paralysis; in the retina with amblyopia; in the pancreas with hemorrhagic pancreatitis, etc. In proportion to the amount of damage sustained by the kidneys in malaria there is less tendency for parasites in pernicious attacks to accumulate in these organs than in any other of the body. The most carefully studied case of this condition is that of Ewing.[35]

These localizations consist in the main of parasite-infected red blood cells; there may be, however, pigmented leucocytes and free parasites and pigment. The parasites in each particular case may be of the same or of different stages of development. The pigmented and sporulating forms are probably oftenest seen, but the earlier phases are frequently observed. It would seem reasonable that the crescents, on account of their size, would frequently form an important element in these accumulations of parasites, but such does not appear to be the case.

The cause of these parasitic concentrations is problematical. It cannot be due to the size, weight, or loss of elasticity of the infected cells, for, as Mannaberg[3] states, the benign parasites would be more apt to form thrombi if this were the cause. Kelsch and Kiener[36] and others have observed endothelial swellings in the small cerebral vessels with consequent construction of caliber, but whether this is a cause or an effect cannot be said. Vasomotor influences and phagocytosis have also been invoked in explanation. The most probable theory is that of Mannaberg[3] who attributes the condition to a sort of agglutination or adhesiveness that holds the infected erythrocytes to the vessel walls.

The symptoms present in cases in which, on post-mortem examination, localizations of parasites are demonstrated, are not always referable to these aggregations alone, since changes are frequently observed which are secondary to parasitic thrombosis and may outweigh the latter in pathogenic importance. The most conspicuous of these changes are perivascular exudation, hemorrhage, and necrosis. The hemorrhages are usually punctate, but Blanc[37] and Ziemann[26] report large cerebral clots.

This propensity of the parasites in pernicious fever to congregate undoubtedly explains the course of many cases but by no means all. Fatal cases of comatose malaria have been observed with no parasites at all in the brain. Ford[38] reports a case with serious pulmonary symptoms in which the parasites were no more numerous in the lung than in the general circulation. "The severity of the renal lesion with the absence of parasites in the renal vessels also requires mention." [39]

It is not known whether parasitic thrombi may exist without producing symptoms. Frerichs,[10] who frequently observed thrombotic occlusions of the cerebral vessels insisted that too much stress should not be laid on them on account of the rich collateral circulation. He likewise affirmed that he had more than once seen markedly pigmented brains without cerebral symptoms during life.

From the study of a case in which the patient was suddenly attacked with transient coma three times in five days, Ewing[39] believes that embolic processes are factors in some instances. This is the most probable explanation of these cases.

Toxins.—The existence of a toxin, the product of the malarial parasite, is almost universally assumed by students of malaria. The grounds for this assumption may be briefly recounted as follows:

1. An analogy with other infectious diseases.

2. Immunity. This immunity is not absolute, but that a relative immunity to malaria exists there is no room for doubt.

3. The formation of an antitoxin. Ford's[40] experiments are nothing short of conclusive of the existence of an antitoxin.

4. Degenerative changes in the kidney, liver, spleen, and other organs, not otherwise explainable.

5. Blood changes, as anemia out of proportion to the number of parasites, and brassy degeneration, stippling, and polychromatophilia of the red cells.

6. Increased toxicity of the urine and sweat.

7. The existence of coma in malaria without parasites or pigment in the brain.

8. The fever and its relation to parasitic sporulation.

9. Experimental proof. The negative results of Gualdi,[41] Montesano,[41] Mannaberg,[3] and Celli[1] are devoid of weight against the convincing experiments of Rosenau, Parker, Francis, and Beyer,[42] who demonstrated the existence in malarial blood of a poison capable of reproducing the symptoms of the disease when injected into the veins of other men.

Individual Predisposition and External Etiological Influences.—"We ought then, in cases of pernicious fever, to seek in the conditions of the ground whose quality is so different, and not in the quantity of the seed, the reason which shall explain to us the gravity of the disease."[43]

The quality of the soil, in the sense so aptly employed by Homem, as a factor in the pathogenesis of pernicious malaria, has probably not received the attention it deserves. This influence in many instances doubtless not only induces the attack but determines its type. Organs or systems enfeebled by antecedent ailments are apt to play the title rôle in the pernicious tragedy. Thus algid and choleraic attacks may be associated with a history of intestinal catarrh; the comatose and delirious cases with a history of abuse of alcohol; the convulsive with epilepsy, etc. It is not improbable that some cases of dysenteric, cardialgic, syncopal, tetanic, cataleptic, paralytic, pneumonic, pleuritic, gastralgic, and other forms described by the older writers may be similarly explained. Mercier[44] goes so far as to say that all pernicious attacks are merely visceral complications.

Malarial subjects who are much exposed to the heat of the sun are liable to be stricken with pernicious fever, especially of the cerebral type. This danger is enhanced if to the solar heat are added fatigue, deficient or improper food, or other hardships. Certain psychic states have causative significance. Hertz[45] states that he has seen the localization of pernicious symptoms determined by injuries of the skull through a fall or a blow.

In addition to the four principal factors enumerated, congestion of viscera and parasitic obstruction of the hepatic capillaries have been regarded as important. It is probable that they have little influence.

A feeble phagocytic activity was considered by Golgi as predisposing to pernicious attacks. In the present state of our knowledge it is impossible to define the relation of this function to perniciousness.

A consideration of the relative frequency with which the several factors are concerned in the pathogenesis of the various forms of pernicious malaria will necessarily be brief. In the comatose variety any of the four chief agents may take part; idiosyncrasy and external influences may unite with any of the other factors; an extraordinary number of parasites in the general circulation without accumulation in the brain is productive of coma probably because of the toxin. Ewing[39] says that the majority of cases of comatose malaria coming to autopsy do not show a massing of parasites in the brain. He attributes these cases to general toxemia. However a study of the autopsy records of Marchiafava and Bignami[2] shows that in a great majority of their fatal comatose cases the parasites were markedly localized in the brain. Davidson[17] and Ruge[46] believe that almost always the cerebral capillaries are found filled with parasites in those who have died with coma.

Other pernicious cerebral forms are usually associated with parasitic localizations.

The algid variety, while possibly sometimes dependent on toxemia, is usually due to a massing of the parasites in the gastrointestinal mucosa. This is explained by Davidson[17] as follows: "Experiments show that the alimentary tract is in closer connection with the cardioinhibitory center than other parts of the body, and that irritation of this tract, if sufficiently powerful, will produce cardiac inhibition, with pallor of the surface and accumulation of the blood in the abdominal vessels. That the intestinal canal is the center of mischief in this form of pernicious attack will appear all the more probable if we observe the character of the disturbances so frequently associated with the algid condition—the cardialgic pain, the choleraic vomiting and purging, and the dysenteric discharges."

Other forms of pernicious malaria are probably due to localization or to complications.

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REPORT ON A PECULIAR DISEASE OF TROPICAL AFRICA CALLED "ONYALAI." *

BY F. CREIGHTON WELLMAN, M.D., BENGUELLA, WEST AFRICA.

During the three or four years that have elapsed since the writer first reported the existence of the disease called by the Umbundu-speaking natives of Angola "Onyalai," several workers have written concerning the same or a similar affection, and a *résumé* of these observations may be helpful. Since my first note I have studied several additional cases with the object of determining the cause of the various symptoms, and the data relating to these are here presented for the first time.

HISTORICAL NOTE.

1. The first mention of the disease was, I believe, my initial note published early in 1904. In this I stated that hemorrhagic bullæ are a feature of the trouble and added the following:[1] "Onyalai" is "a common and very treacherous disease, greatly feared by the natives, considered by them very fatal. I was once disposed to treat the native view very lightly, but after seeing cases die from it in a few hours from the beginning of an attack, I revised my notion. The bullæ may be small and affect only the surface of the body, or occur only on the tongue, soft palate or buccal mucous membrane. When large and involving the esophagus and pharynx they may cause trouble, but when they occur in the brain, its

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membranes, or even in the important abdominal viscera, death often results. The size of the bullæ varies markedly, ranging from that of a split pea to that of a half crown piece." Later [2] I repeated this note and added that " the disease is not pemphigus, *Dermatitis herpetiformis*, nor the affection known as *Epidermolysis bullosa*. The bullæ appear suddenly after an initial period of malaise. . . . The vesiculation is rather deep and, when occurring in the skin, always involves the corium. The bullous formations contain trabeculæ, the interstices of which are filled with partially coagulated blood, to which their dark colour is due. The disease generally disappears (if death does not occur) as suddenly as it came."

2. Massey [3] published, subsequent to my preliminary note, the record of three cases of " Onyalai " seen by him in Angola. These cases all had symptoms similar to those detailed by me and all recovered. Massey states (what coincides with my experience) that the blacks are very much afraid of the disease, regarding it as most fatal. He treated his cases with bicarbonate of soda and cod liver oil.

3. Feldman [4] has mentioned a disease among the natives of Bukoba in East Africa and called by them " Edjuo " which Mense [5] is inclined to connect with " Onyalai." Feldman noticed stomatitis and swelling of the parotid glands in connection with his cases.

4. Mense [6] observed during his stay on the Kongo a disease, called by the Unyamwezi people " Kafindo " which spread across equatorial Africa and which was marked by depression, malaise, headache, reddened conjunctivæ, numbness, swelling of the tongue, loss of appetite, and occasional bloody diarrhea, dyspnea, cardiac disturbances, etc., all of which symptoms I have

seen in my cases of " Onyalai." Mense states, however, that the peculiar bullæ described by me were not noticed in his cases. He did not personally observe any cases that terminated fatally, but such were reported from East Africa. He differentiates " Kafindo " from dengue and other diseases and discusses its possible connection with poisoning with Euphorbiaceæ and other native plants. Mense in conclusion mentions the native treatment, which consists of scratching the tongue until bleeding occurs, and that of the missionaries (phosphorus, essence of bee venom) and recommends for the stomatitis astringent mouth washes.

It is not absolutely certain that these several observations all relate to the same disease, but it is very probable that they deal with identical or closely related affections. I know of no other literature on the subject.*

ETIOLOGY.

Obscure. Following are notes on some of the investigations I have made regarding this point. The results of my inquiry are largely negative and may be stated as follows:

1. " Onyalai " is not a manifestation of malaria. While the hemorrhagic and other symptoms of the affection under discussion are not unknown in malarial processes, yet I consider that I have excluded this infection as an etiologic factor. I base this statement on the following data: None of my first 8 cases had any enlargement of the spleen and but three of them showed

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* Maxwell (*Journal of Tropical Medicine*, July 1, 1901, p. 211) has reported hemorrhagic bullæ of the mouth and pharynx seen by him in Changpo, South China. These, however, probably have no connection with " Onyalai " since, according to Maxwell, the bullæ are confined to the oral cavity and are accompanied by no systemic symptoms. The Chinese attribute the bullæ to the accidental introduction into the mouth of a certain kind of spider web.

rise of temperature. These 3 were examined for malarial parasites but none was found. None of my 5 recent cases showed enlargement of the spleen. Only one of them showed malarial parasites in the blood. In another case I found some pigmented leukocytes. This case, however, had just come from a very malarious district and I had administered to him large doses of quinine for some days. None of the other cases had had quinine. Twelve of the 13 cases were suddenly taken ill while in robust health. Also 12 out of my 13 cases were males. Two of Massey's cases were males. The sex of the third is not given. Nearly half of the cases had experienced the same trouble before. In two instances two members of a family were affected and in four instances more than one case came from the same house. All these facts suggest to my mind something very different from malarial infection which is almost universal among Africans while " Onyalai " is comparatively rare. While preparing my recent report to the *Società per gli Studi della Malaria,*[7] I examined microscopically the blood of over 500 natives and took the spleen index of as many more, and I find on comparison that my cases of " Onyalai " were rather freer from the signs of malaria than the average native of my district.

2. " Onyalai " is not accidental or purposed poisoning. I have had occasion to study the various substances included in the poison test [8] and those formerly used to poison arrows [9] as well as the medicinal plants employed by the blacks of this district [10] and the symptoms set up by poisoning with any of these are radically different from the clinical picture presented by a case of " Onyalai." A case of snake bite from the puff adder (*Clotho arietans,* Gray) which I

reported some time ago[11] simulated some cases of "Onyalai" very closely, but my patients had none of them been bitten by snakes.

3. Trypanosomes and other organisms were searched for with no result. On two occasions I cauterized the surface of large bullæ and cut down on the inclosing clot, removing a piece of the same and dropping it into sterile broth. Such cultures remained sterile.

4. "Onyalai" is easily and sharply distinguished from Schönlein's disease by the absence of the multiple arthritis, eruption, etc., and from Henoch's purpura by its frequency in adults and acute course. It cannot be identified with *Purpura hemorrhagica* as it occurs oftenest in robust and adult males. It must be emphasized, too, that the superficial hemorrhagic bullæ are by no means to be considered the only nor indeed the chief factor in the disease, for, as will be shown later, I have seen two fatal cases of what I believe to be this ailment in whom no bullæ were visible, either on the skin or mucous membranes. In other cases they were so small and few in number as to be easily overlooked. There do not occur to me any other diseases for which "Onyalai" is likely to be mistaken.

To sum up: I am inclined to consider "Onyalai" a specific entity, in other words an acute infectious disease the cause of which is as yet undetermined.

CLINICAL FEATURES.

Most of my cases were attacked suddenly. Lassitude and a sort of dazed appearance was generally marked. In some cases the parotid glands were tender to the touch. The eyes appeared heavy and sometimes reddened. In most instances the tongue was swollen and painful.

A slight temperature was noted in about a third of the cases. I have had patients complain of numbness and of pain in various parts of the body. One man who had bloody diarrhea suffered much from colicky pains. The appetite is usually poor. The bullæ may appear in the mouth, pharynx, esophagus, stomach and bowels. Vomiting of blood is not rare. The skin also usually shows lesions. The genito-urinary system was affected in 3 of my cases. Hematuria was a prominent symptom in all of these. When the process occurs in the cranial cavity various symptoms of profound central disturbance are set up. Three cases of this kind have come to my attention. One of these was a young woman in rude health. She was laughing and playing on the evening of her attack. Suddenly she complained of being tired, and in an hour or so bullæ appeared in her mouth. She steadily grew more depressed and died about eight o'clock the next morning with all the symptoms of cerebral hemorrhage, *i. e.,* loss of consciousness, inactive, dilated pupils, slow, noisy, stertorous breathing, etc. The pulse was very slow and increased in tension. Another fatal case in the same house, a strong young man being the victim, presented almost exactly the same symptoms. A third fatal case showed no vesicles, either in the mouth or in the skin. The feces and urine likewise contained no blood. Another case which I have also referred to this disease also showed no vesicles, but died from the effect of what I believe to be the same process in the liver, spleen and pancreas. (These last two cases were shown microscopically not to be pernicious malaria.) The superficial bullæ when present are characteristic. They range from the size of a split pea to several inches in diameter. The larger ones are irregular in outline and are often umbilicated. They are deep and involve the corium or submucous structure. There seems to take place an extensive histolysis, only the fibrous elements persisting. These appear as trabeculæ, the interstices of which are filled with partially coagulated and otherwise altered blood which shows dark under the skin or mucous membrane. The red corpuscles, however, are not all disintegrated, and may be seen under the microscope in the oozing from the blebs and also in the feces, urine, saliva, etc., according to the situation of the lesions. In one or two cases the bullæ were very small and not numerous, and had the patients not directed attention to them would probably have been overlooked.

PROGNOSIS AND TREATMENT.

My series of cases is yet too small to admit of general statements. As has been said, the natives consider "Onyalai" to be a very fatal disease and tell of instance after instance that have terminated in death. Of the 13 well authenticated cases studied by me 2 died. To these should probably be added the 2 cases previously mentioned which showed all the symptoms of the disease excepting the characteristic bullæ. The malignancy of the disease varies greatly, judging from native reports, some seasons and districts exhibiting many more fatal cases than others. It should be said that the trouble has a tendency to recur. I have seen one man who has suffered three attacks and another who has had two. The relapses seem to occur a few months apart.

As to treatment I am not prepared to be dogmatic. The natives employ various plants, prominent among which is *Geigera wellmani Hutch*, and a species of Albizzia (*A. anthelmintica* A. Brong.). I have personally tried quinine, various alkaline salts, oil of turpentine, acetate of lead, tannic acid, ergot and suprarenal extract with no perceptible results. I am inclined to think that arsenic in full doses has benefited some cases.

In conclusion I should be pleased to hear from any colleague who has met with the disease.

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NOTES ON DENGUE IN CUBA.

By A. H. Allen, M. D.,
Lajas, Santa Clara, Cuba,
Assistant Surgeon, United States Navy.

(Published under the Imprimatur of the American Society of Tropical Medicine.)

The towns of Lajas and Santo Domingo are situated about forty miles from the sea coast in the interior of Santa Clara province. Mosquitoes are abundant during the entire year, the most frequent species being the stegomyia, culicidæ, and anopheles, in the order named.

In August of 1907 I observed some cases of dengue fever which are reported on account of their mild character and failure to assume an epidemic form. In all, there were eighteen admissions to the sick list in two companies of United States marines stationed in the two towns mentioned.

Incubation.—The incubation period in one patient was three days, in two patients four days, in the others unknown, but probably not over three or four days.

Prodromes.—There were no prodromal symptoms, the first sign of the disease being frontal headache and vertigo, which were pronounced. Pain in the eyeballs was a prominent symptom in every case. Only one patient had severe pain in the joints, although six complained of pain in the loins and back, and all complained of a very slight rachialgia. One patient had abdominal pain with vomiting and diarrhœa, which lasted for twelve hours. In all patients

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the digestive system showed only the ordinary signs of the febrile state. In no case was pain a prominent feature.

Defervescence started on the first or second day, without crises of any kind.

Rashes.—The rash appeared on the second or third day. The so called "primary" rash was present in five cases. The face was flushed and the mucous membranes of the nose and throat were somewhat congested. The conjunctiva was slightly reddened. This condition disappeared in from twelve to twenty-four hours, either before or during defervescence, and was succeeded by the typical rash. This eruption showed a preference for the dorsal surface of the forearms, internal surface of the thighs, and the back and chest. It was present in all cases. Its character was discrete, roundish maroon, or reddish spots from one quarter to three quarter inches in diameter, slightly raised. On the forearms and thighs the spots rapidly coalesced; on the back and chest they remained comparatively discrete. In one case the rash on the arms and neck gave the appearance of a severe sunburn. Fading took place in from twelve to twenty-four hours in the majority of cases, although in one the rash persisted for seventy-two hours, and in three for forty-eight hours. A very slight furfuraceous desquamation succeeded its disappearance.

Glands.—In three cases the superficial cervical glands were enlarged. In fourteen cases the inguinal glands became swollen without pain, although the fact that most of these patients had a previous venereal history must be noted.

Temperature and Pulse.—The highest temperature was 103° F., which occurred on admission, the average being about 102.2° F. The pulse was uniformly low. With fever of 103° F. the pulse was 92; with temperatures of 102° F. in six cases the pulse varied from 80 to 100. The highest pulse rate was 102.

Blood.—No blood examination was possible, as there was no microscope available, and the United States Army Hospital at Cienfuegos, Cuba, was contending at the time with an outbreak of yellow fever.

There was no albuminuria or any tendency to hæmorrhage in any case.

Transmission.—The theory of Graham and Bancroft, who consider the mosquito the infective agent, seems to receive some corroboration in these cases. In previous reports the presence of one case of dengue is soon followed by an epidemic. In these cases the barracks were fumigated with sulphur dioxide to destroy all infected insects, and the use of the mosquito bar was rigidly enforced. The patients were immediately removed to a screened building and treated under mosquito nets. One case of a hospital apprentice, who nursed the cases and was attacked with a typical seizure of the disease three days later, was thought to be due to lack of care in the use of the bar, as another apprentice, doing the same work, yet protecting himself securely at night, was not attacked with the disease.

Conclusion.—In summing up, the most noticeable features of the cases were the uniformity of the rash, the very slight amount of pain associated with the disease, the comparatively low pulse, the mild character of all cases, and the possibility of the mosquito being the transmitting agency of dengue.

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INTERIM REPORT ON TRYPANOSOMIASIS IN PORTUGUESE SOUTHWEST AFRICA.

BY

F. C. WELLMAN,

of Angola, Africa.

Published under the imprimatur of the American Society of Tropical Medicine.

As I have pointed out on other occasions trypanosomes of both man and animals in the high, cool tableland of Portuguese West Africa, have been difficult to find, and probably a smaller percentage of infections obtains than in lower-lying regions. I have, however, continued to examine, with this parasite in mind, the blood of a series of natives and also to examine the blood and tissues of whatever animals I could obtain. When trypanosomes were first demonstrated in birds and in man, I hoped to carry through at once a series of inoculation and cultivation experiments with the parasites. Pressure of other work has, however, prevented my completing such investigations and I have thought best, having published preliminary notes on the subject, to present this progress report of observations made to date, leaving the incompleted experiments to be detailed in a subsequent communication.

The district in which the following investigations were made, lies about Lat. 12° by Long. 16°. The altitude, at the point where the most of them were carried out, is 4,761 feet.

I do not know of any mention in medical

literature of trypanosomes from West Africa south of the Coanza river prior to my communication dated July 25, 1905, and entitled "Preliminary Note on a Trypanosome. Found in the Blood of an African Dove (*Treron calva*)." Later (September 14, 1905), I sent a second note, also of a preliminary character, entitled "Human Trypanosomiasis in Portuguese Southwest Africa" to the secretary of the American Society of Tropical Medicine in which I mentioned (beside the trypanosome just noted) two cases of human trypanosomiasis, the first of which was seen on August 19, 1905, and a second bird trypanosome found since the publication of the initial note.

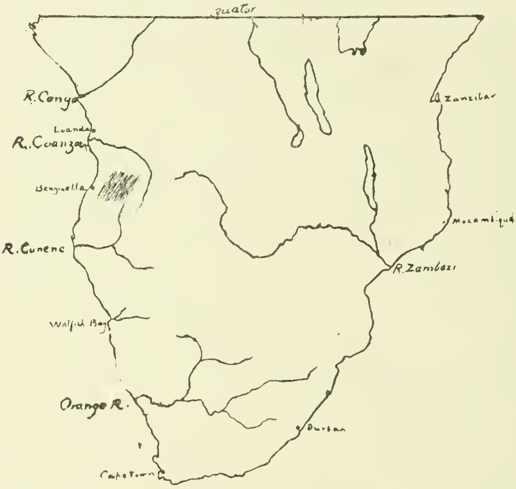

FIG. 1.—Map of South Africa. The shading shows the district mentioned in this report.

The following table shows the number of

species and the number of individuals of each species the blood of which has been examined for trypanosomes.

TABLE I.

No.	Name of animal studied.	Number of individuals examined.	Number of individuals affected.
1	Man	531	3
2	Monkey (*Cynocephalus*)	4	0
3	" (*Cercopithecus*)	7	0
4	Lemur	1	0
5	Bat	3	0
6	Cat	4	0
7	Dog	11	0
8	Rat	19	1
9	Ox	6	0
10	Goat	13	0
11	Sheep	4	0
12	Antelope (*Cervicapia bohor*)	2	0
13	" (*Cephalolophus grimmi*)	1	0
14	Pig	9	0
15	Horse and Mule	11	0
16	Owl (*Athens perlata*)	1	0
17	Wagtail	1	0
18	Crow (*Heterocorax capensis*)	1	0
19	Gray Parrot (*Psittacus erithacus*).	2	0
20	Green Paroquet	5	0
21	Dove (*Treron calva*)	9	2
22	Sand Grouse (*Pterocles sp.*)	2	0
23	Domestic Fowl	8	0
24	Ox Bird (*Buphaga africana*)	1	0
25	Plover	1	0
26	Sand Lizard (*Acontias maleagris*)	4	0
27	Snake (*Viper*)	1	0
28	Frog	6	1
29	Tree Frog	1	0
30	Brook Fish (*sp.?*)	13	0
31	Snail	3	0

The following table shows the number of species of trypanosomes found and the species and number of individuals of each species ot animal infected by them.

TABLE II.

No. of species of trypanosomes	Name of infected animal.	No. of infected individuals studied.
1	Wild Dove (*Treron calva*)	2
2	Man.	3
3	Rat	1
4	Frog	1

DESCRIPTION OF TRYPANOSOMES FOUND.

Trypanosome 1.—This trypanosome (see Plate II, Fig. 7) resembles rather closely *Tr. avium*, Danlewsky. Slight differences from the typical form might be said to exist but as I have not yet made cultivation experiments to determine if its cultural forms bear out these delicate distinctions, I class it for the present with the species above mentioned with which it will probably prove to be closely related if not identical. The trypanosome as seen in the blood of the wild dove is a plump fish-shaped body, rather sharp at the posterior end. Faint longitudinal striæ or myonema lines can be made out in the protoplasm as well as very fine granules. The nucleus extends about two-thirds across the body and seems almost completely to fill the space in which it lies. The flagellum and undulating membrane are wavy in very regular curves. The free flagellum is comparatively short. Following are the principal measurements of a stained specimen: Length (about), 28 microns; greatest width, 9 microns; distance of centrosome from posterior end, 4 microns; length of free flagellum (about), 8 microns; longest diameter of nucleus, 6 microns.

Trypanosome 2.—This trypanosome (see Plate I, Figs. 1–2) seems to be morphologically identical with *Tr. gambiense*, Dutton. The posterior end is truncated and the arrangement of the centrosome, nucleus, and flagellum as well as the "set" of the organism on the slide correspond closely with the same points in *Tr. gambiense*. The protoplasm stains somewhat irregularly with Romanowsky, taking on a basophile reaction. The centrosome stains a dark purple hue and the flagellum (which stains pink) seems to rise from or near it. Anterior to the centrosome lies the vacuole. The nucleus lies near the middle of the body and often occupies more than two-thirds the width of the parasite. It is oval in shape and stains red like other chromatin material. Following are the measurements of a stained specimen: Length (about),

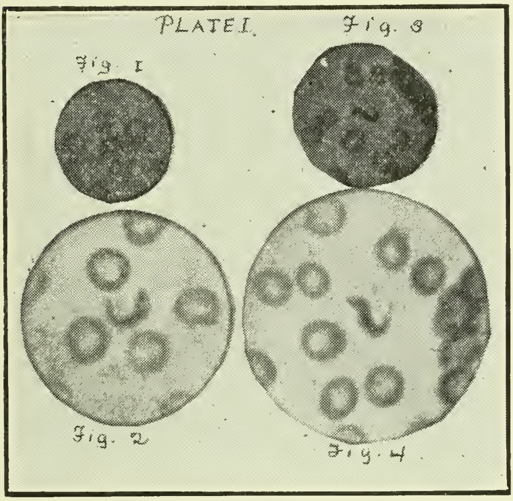

PLATE I.
FIGS. 1 and 2.—*Tr.* (?) *gambiense* in man.
FIGS. 3 and 4.—*Tr.* (?) *gambiense* in dog.

24 microns; greatest width, 3.5 microns; distance of centrosome from posterior end, 3 microns; length of free flagellum (about), 9 microns; largest diameter of nucleus, 4 microns.

Trypanosome 3.—(See Plate II, Figs. 5–6.) Very probably *Tr. lewisi.* No differences in structure from those characteristic of that species can be made out in my specimens. The slender contour and narrow undulating membrane are well shown. I give measurements of a stained specimen. Length (about), 25 microns; greatest width, 2 microns; distance of centrosome from posterior end, 4 microns; length of free flagellum (about), 10.5 microns; largest diameter of nucleus, 3 microns.

Trypanosome 4.—(See Plate II, Fig. 8.) Resembles rather closely *Tr. mega*, Dutton and Todd. This same parasite or a very similar one has also been found on the Congo. The distinguishing points of this trypanosome are the great size, the longitudinal markings, the great distance of the centrosome from the posterior end, the ill-defined nucleus and the tortuous flagellum. Following are the measurements of a stained specimen: Length (about), 60 microns; greatest width, 8 microns; distance of centrosome from posterior end, 17 microns; length of free flagellum (about), 18 microns; largest diameter of nucleus, 3.5 microns.

Cases of Human Trypanosomiasis.

Case I.—This is the case mentioned in my preliminary note on human trypanosomiasis. Name. Chimbomba. Age, 30. Sex, male. Race, Bantu (Chiyaka tribe).

History.—This man was examined in an unselected series of natives. Gave no history of illness except occasional slight fevers. Has frequently been in Esupua (the tsetse fly belt of the district).

Condition when Examined.—There were no symptoms whatever that would lead one to suspect trypanosomiasis. The temperature was normal. A hematokrit of the blood showed about 5,000,000 red cells and 7,000 leukocytes.

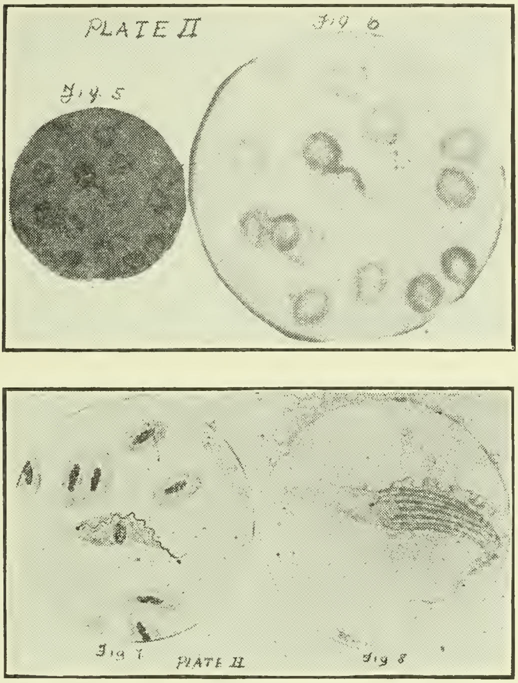

Plate II.
Figs. 5 and 6.—*Tr. lewisi* in rat.
Fig. 7.—*Tr.* (?) *avium* in dove.
Fig. 8.—*Tr.* (?) *mega* in frog.

A feces examination revealed only the presence of a few ova of *Ascaris lumbricoides*. Urine normal. A differential leukocyte count showed the following results:

Note.—Specimens of each of the trypanosomes figured have been sent to the secretary of the American Society of Tropical Medicine with this report.

About 500 cells counted. Polymorphonuclears, 31 percent; lymphocytes, 25 percent; large mononuclears, 24 percent; transitional, 7 percent; eosinophiles, 13 percent.

I have frequently seen as great a proportion of large mononuclear and eosinophile leukocytes as this count shows in West African Bantus enjoying the best of health. Trypanosomes were abundant in the peripheral circulation and in preparations obtained by aspirating the cervical lymphatic glands, which glands, however, were not enlarged and seemed in other respects normal. The man would not consent to lumbar puncture so I was not able to examine the cerebrospinal fluid.

CASE II.—Name, Wele. Age, 23. Sex, male. Race, Bantu (Chiyaka tribe).

History.—Had suffered for several months with irregular fevers which were milder and rarer at the time I saw him than they had been formerly. He has frequently been in the fly belt (Esupua).

Condition when Examined.—Patient was thin and there was marked edema of the eyelids. The skin was harsh and dry. A papular eruption somewhat resembling recently acquired scabies was present on the back, arms, and thighs. The cervical glands of the right side were very slightly enlarged. Tongue was coated, pointed, and tremulous. Feces contained ova *Uncinaria* and *Ascaris*. Urine was normal. Several large blood films were searched and one typic trypanosome was seen with several pear-shaped undifferentiated forms. Only fresh films were available and the patient could not be persuaded to leave his village.

CASE III.—This case was reported to me by Mr. W. E. Fay, of Chilume, a place three days distant from the point where this paper is written.

Name, Kasoma. Age, 28. Sex, male. Race, Bantu (Bailundo tribe).

History.—About one year ago he had fever and pains in the bones of the legs for several weeks. Has been well since. Has often been in Esupua.

Condition when Examined.—Blood showed infection with malarial parasites as well as trypanosomes. Spleen enlarged, reaching half way to the umbilicus. Face showed a puffy appearance caused by slight edema. No skin eruption. In other respects the man was in good health and condition.

Inoculation Experiments with Tr.(?) Gambiense.

Animals suitable for inoculation experiments were very difficult to obtain. Monkeys, guinea-pigs, etc., were impossible to procure. The following animals were inoculated from Case I: 1. Three dogs. 2. One goat. 3. One rat.

The rat died the ensuing night. The goat and two of the dogs (a pure bred English fox terrier and a dachshund from Germany) showed no evidences of infection and no trypanosomes could be found in their blood. The third dog (a mongrel) showed parasites at the end of one week, but evinced no signs of illness and retained its condition perfectly. Small pear-shaped forms (see Fig. 2 f.) were also seen in its blood. The parasite as seen in this dog showed on

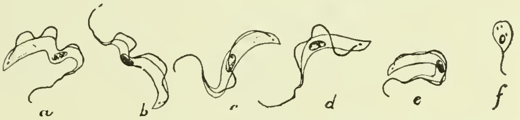

Fig 2.—*Camera lucida* outlines showing (*a–b*) different positions assumed by *Tr. ? gambiense* in stained preparation; *f*, pear-shaped developmental form.

the whole a blunter and plumper contour than it assumes in the human subject. (See Plate I, Figs. 3–4.) This dog escaped a few days after the parasites appeared in its blood and was never found. It was found impossible in view of the disadvantageous circumstances under which I worked to make cultivation tests. These, with fuller inoculation experiments, I hope to carry out at some future time.

POSSIBLE CARRIERS OF TRYPANOSOMES IN THE DISTRICT.

1. In view of recent researches it is probably safe to say that the local spreader of human trypanosomiasis is the only tsetse fly of the district, *Glossina palpalis wellmani*, Austen (*sub-sp. nov.*). The "fly belt" of the region through which all porters from the interior must pass in order to reach the coast, and which swarms with *Gl. palpalis wellmani*, is at a point called Esupua. In all three cases of human trypanosomiasis I have mentioned, the patients gave the history of having been frequently in Esupua. I hope shortly to publish a detailed study of the morphology and bionomics of *Gl. palpalis wellmani*, and shall not, therefore, include here what can be better and more fully treated in a separate paper, and what from its importance deserves special discussion.

2. The hemophagous larva of *Auchmeromyia luteola*, Fabricius, is of possible interest in connection with the general subject of trypanosomiasis in mammals. I have recently published a study of this fly (with drawings) and refer the reader to my paper mentioned in the bibliography appended to this report.

3. The Ochihopio Tick (*Ornithodoros mon-*

bata, Murray) may also be mentioned here. It has been proved to carry *spirochætæ* and should not be lost sight of, as it preys on all warm-blooded animals. I have described and figured this tick in another place (see bibliography).

4. *Tabanidæ* and other biting flies. Observations in India and the Philippines on animal trypanosomiasis forbid us to exclude biting flies other than *Glossinæ* from an account of the possible transmitters of the disease. The *Tabanidæ* of this region are quite peculiar to themselves and my collections contain a number of flies new to science. These are of the species *Tabanus*, *Hæmatopota*, and *Chrysops*. One common *Tabanus* is *T. rubeicundus*, Walker, or a closely allied species which I figure below (Fig. 3) and another is probably a new species (near *latipes*, Macq). Ten or a dozen species of *Hæmatopota* have been collected most of which are new. The other Tabanid fly of the region is *Chrysops* of which there are several species not yet determined. I should not neglect, while speaking of biting flies, to state that several species of Stomoxys are common.

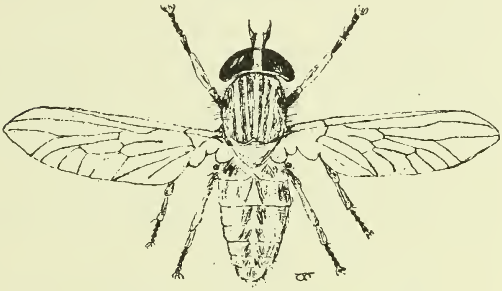

FIG. 3.—*Tabanus ? rubricundus*, Walk.

Conclusions.

The main results of the foregoing investigation may be briefly stated as follows.

1. Trypanosomiasis of *Batrachia*, birds, rodents and man extends at least as far south on the west coast of Africa as Benguella.

2. The species found in southern Angola at an elevation of nearly 5,000 feet differ very slightly as regards morphology from those found on the coast farther north (Gambia, Congo).

3. About three natives out of every 500 in southern Angola show in their blood a trypanosome which is *Tr. gambiense* or a closely allied form.

4. The clinical symptoms of such trypanosomiasis are mild and ill defined. (No cases of sleeping-sickness originating in the district have been seen.)

5. Other animals (dogs) are susceptible to artificial infection with this human trypanosome. The symptoms of such infection in dogs are probably very slight or wanting.

6. The probable carrier of the human trypanosome is *Glossina palpalis wellmani*, Austen (*sub.-sp. nov.*)

7. The transmitters of the frog, bird, and rat trypanosomes are as yet undetermined.

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Extracted from the American Journal of the Medical Sciences, September, 1908

OBSERVATIONS ON THE HYPODERMIC USE OF QUININE AND UREA HYDROCHLORIDE IN THE DIAGNOSIS AND TREATMENT OF ACUTE AND CHRONIC MALARIAL INFECTIONS,

AND ON THE RESEMBLANCE TO THE SEXUAL CYCLE OF THE HEMAMŒBA MANIFESTED BY THE PERIODS OF FREEDOM FROM PAROXYSMS THAT ORDINARILY FOLLOW A SINGLE INJECTION OF ABOUT ONE GRAM OF THIS SALT.[1]

By Solomon Solis Cohen, M.D.,
PROFESSOR OF CLINICAL MEDICINE IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA;
PHYSICIAN TO THE JEFFERSON MEDICAL COLLEGE HOSPITAL AND THE
PHILADELPHIA GENERAL HOSPITAL.

The object of this paper is to recall attention to four points in connection with the hypodermic use of quinine and urea hydrochloride in acute and chronic malarial infections: (1) The superiority of this salt over other preparations of quinine. (2) The periods of either six and one-half days approximately, or thirteen days approximately, during which patients previously exhibiting irregular recurrences of paroxysms, or regular quotidian, tertian, or quartan recurrences, remain free from paroxysms following a single injection of about 1 gram (15 grains) of this salt. (3) The similarity between these periods of six and one-half and thirteen days respectively, and the periods of cyst formation and of sporozoite development in the sexual cycle of the parasite, as observed in the mosquito. (4) The diagnostic value of such injections, both in proving and in disproving malarial infection in cases in which parasites have not been discovered in the peripheral blood.

A fifth point may be emphasized in passing, as a variant of the first, namely, the probable therapeutic superiority of this quinine salt in pernicious malaria.

In connection with the similarity between the significant periods of the sporogony of the hemamœba and the week and two-weeks freedom periods following the use of quinine in this active form, I have sought, and had search made, for gametes and sporozoites, but without success. I am extremely desirous that the observations should be repeated by observers more skilled in technique and in parasitology, than I and having more continuous control of abundant material.

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[1] Read by title at the fifth annual meeting of the American Society of Tropical Medicine, Baltimore, March 28, 1908.

My experience with the use of the double hydrochloride of quinine and urea in the treatment of malarial infections dates from 1884, when I was chief of clinic in the Medical Out-patient Department of the Jefferson Medical College Hospital, in the service of Professor Roberts Bartholow, whose praise of this preparation led me to its use. Its advantage is extreme solubility, as it dissolves in its own weight of water, thus making possible the administration of a sufficient dose, which is quickly absorbed. Its disadvantage is the liability to produce slough or abscess if one is not careful in the use of the preparation. With due care to make the injection deeply under the skin, but not necessarily into the muscle, and to empty the syringe before withdrawing the needle, so that no drop of the solution shall fall upon the integument as the needle leaves the tissues, such accident need not be feared. An additional precaution invariably employed in my service is to seal the point of puncture with iodoform collodion or with tincture of iodine.

In G. E. de Schweinitz's experiments[2] upon quinine amblyopia, he found the quinine and urea salt much more toxic than any of the other preparations which he employed. Incidentally to the therapeutic studies summarized in the following pages, observations have from time to time been made as to the effect of the drug upon leukocytosis. So far as the gross leukocyte count is concerned, it frequently seemed to reduce the number slightly, but this effect was not invariable, nor did the decrease persist for more than forty-eight hours after the injection. Not rarely, the fall would be followed by an increase above the previous figure. As to differential counts, the observations are insufficient and inconclusive.

Acute Malarial Infection.—The observations which here are summarized have been carried out in private practice, at the Jefferson Medical College Hospital, both in the Out-patient Dispensary and in the wards, and at the Philadelphia Hospital. Unfortunately, some of the records have been mislaid, so that accurate statistics cannot be given. Approximately, there have been treated by this method about 250 cases of acute malarial infection, of which 1 was of quartan periodicity, upward of 100 of quotidian periodicity, and upward of 140 of tertian periodicity, the remaining 5 or 6 exhibiting irregular recurrence. In the 1 case recorded as of quartan periodicity the parasite was identified as the quartan parasite (Hæmamœba malariæ). In the others the tertian parasite, of the ordinary (Hæmamœba vivax) or estivo-autumnal (Hæmamœba falciparum) type was, in general, recognized. Unfortunately, the records, while noting the presence or absence of organisms, fail to specify in a sufficient number of cases the exact variety found. It is possible that in some cases quotidian parasites were present and not identified.

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[2] Personal communication; also G. E. de Schweinitz, Toxic Amblyopias, Philadelphia, 1896 p. 193

In all cases of which note was made, with the exception of 4 instances in which two injections were necessary to bring about the freedom period, there occurred, following a single injection of 1 gram of the quinine and urea salt, especially if this were administered during the paroxysm or within four hours thereafter, a prolonged, definite period of freedom from paroxysms. In about one-third of the cases this lasted between six and seven days, varying from one hundred and forty-one to one hundred and sixty-two hours; in the remaining two-thirds of the cases, the period of freedom was between twelve and fourteen days, varying from two hundred and ninety to three hundred and twenty-five hours. In some of the case-notes these periods are estimated from the beginning of chill to the beginning of chill, and in some cases from the hour of maximum temperature to the hour of maximum temperature. In future observations a uniform method should be followed. It is also quite possible that nurses on duty do not always catch the exact beginning of a chill, or the exact point of maximum temperature. I am inclined to believe that a fair statement of the average freedom periods would be six and one-half and thirteen days respectively; or perhaps it might be stated as seven and fourteen (week and fortnight) *organism days* of about twenty-one to twenty-two hours each. The most frequent figures to be found in the notes concerning the week-cycle are one hundred and forty-seven, one hundred and fifty, and one hundred and fifty-six hours; in the notes concerning the fortnight cycle, three hundred, three hundred and six, and three hundred and twelve hours. As a rule, but not invariably, the cases showing the shorter period of freedom were quotidian in type. Of those exhibiting the larger period, the preponderating number were tertian. The quartan case showed a freedom period of twelve and three-eighths days, with certain peculiarities, a summary of which is given later.

When the injection is made within less than two hours before the time of an expected paroxysm, it usually does not prevent the occurrence of the chill, although the phenomena are, in general, milder than usual. The paroxysm due to follow will, however, be missed, and the freedom period thereafter be manifested. When the injection is given three or four hours before the time at which a paroxysm is anticipated, it usually prevents the attack. When given between four and eight hours in advance of the expected chill time, the injection will usually prevent both the paroxysm about to be due and its anticipated successor, but sometimes only the latter. The effect cannot be predicted with certainty.

Usually the paroxysms, if tertian, would, after the thirteenth day, resume their former periodicity; or, if quotidian, would, after six and one-half or thirteen days, change to tertian. Rarely did the paroxysms resume the quotidian periodicity. A case of irregular periodicity would assume the tertian, less frequently the quotidian-type. In one instance there is a note made that the paroxysms changed from quotidian to quartan, but as the detailed records are missing and the case dates back to 1885, at which time the specific quartan parasite would not have been recognized, no stress is laid upon this fact.

In other cases, of which 6 are noted (probably all that were observed), after the six and one-half days or thirteen days of freedom, a further freedom period of six and one-half or thirteen days was manifested without further medication; that is to say, the periodicity apparently changed from quotidian or tertian, as the case might be, to what were formerly termed, respectively, the weekly and the fortnightly types. The number of possible observations of this kind was limited, for obvious reasons.

After the occurrence of the freedom period had been demonstrated, and the periodicity of the renewed paroxysms determined, injections were, as a rule, resumed and continued daily in quotidian cases, and on alternate days in tertian cases, until the recovery of the patient was assured; or the drug was administered by the mouth —in capsule—in two doses of 10 or 12 grains (0.75 gram) each, four hours and eight hours, respectively, before the anticipated chill time; or 10 grains (0.65 gram) were given at night and the same quantity in the morning, without special reference to the chill period; or one dose of 20 to 23 grains (1.3 to 1.5 grams) was given between eight hours and four hours before the anticipated chill. On the whole, one method answered as well as another.

When two weeks had passed without paroxysms, the patient was usually dismissed from the hospital, with the injunction to take 20 grains of the drug weekly, in two doses, one of 10 grains on the evening of the sixth day, and one of 10 grains on the morning of the seventh day, calculating from the date of the last paroxysm; and to continue this treatment for at least three months, returning to the hospital or reporting to the Out-patient Department from time to time, for observation.

The case of H. J., observed in October and November of 1907, may be related as a typical instance, illustrating several of the phenomena summarily described (Chart I).

This man had a quotidian intermittent fever, with paroxysms recurring in alternate periods of twenty-one and twenty-four hours. He exhibited the ordinary tertian parasite, and was evidently infected with two broods, maturing at forty-five hours. An injection was given fifty minutes before a paroxysm expected at 11 A.M., on October 26. The chill occurred on time, but its duration was much shortened. The temperature, which in previous attacks had risen to 104° or 105° F., reached only 103°, and fell to the minimum point, 97°, five hours after its maximum had been reached, the fall in previous paroxysms having occupied eight hours. There was no chill on the following day, and the temperature remained practically normal, oscillating between 97° and 98.4° until one hundred and forty-seven hours after the chill, or one hundred and forty-two hours after the temperature had fallen to its minimum. On November 1, the sixth day after the last preceding paroxysm, or the seventh day, including the day of that paroxysm, the temperature rose at 2 P.M. to 102°, remaining elevated for three hours, and reaching normal at 8 P.M., but there was no chill; the paroxysm was incomplete. On November 3, at 9.45 A.M., about forty-three and one-half hours after this incomplete paroxysm, a chill began, and the maximum temperature point of this attack, 104°, was reached at 11 A.M.; that is, about forty-five hours after the maximum point of the paroxysm without chill that had preceded it. The temperature reached its minimum at 8 P.M. A chill occurred at 7.15 A.M. on the fifth of November, again about forty-five and one-half hours after the previous chill, maximum temperature being reached at 8.45 A.M., and minimum temperature not until 2 A.M. the following day. The next chill occurred on the 7th of November at 7.45 A.M., forty-eight and one-half hours after the previous one, maximum temperature occurring at 11 A.M. and minimum temperature at 11 P.M. The fall of temperature was possibly hastened by the second injection of quinine and urea hydrochloride, which was given during the declining stage of this paroxysm, at 2 P.M. No further paroxysm was permitted to occur. The treatment was continued by injections on alternate days until November 16, and the patient left the hospital, apparently well, on November 18.

Examination of the blood had shown the presence of parasites in various stages; hyaline, pre-segmenting, segmenting, intracellular pigmented, and extracellular pigmented forms being present, all in large numbers.

October 24. 200 fields were counted and 600 parasites found.

October 25. A similar count was made.

October 26. 200 fields were counted; 560 parasites were found. On this day an injection was given.

October 27. 200 fields were examined; 12 parasites were found—8 intracellular pigmented and 4 extracellular.

October 29. 200 fields were examined; 3 parasites were found—2 intracellular pigmented and 1 extracellular.

October 30. 500 fields were examined; no organisms were found.

October 31. 500 fields were examined; no organisms were found.

November 1 (the sixth day after the injection). 200 fields were examined; 34 parasites were found—young hyaline, 31; mature intracellular, 2; extracellular pigmented, 1. It was on this date that the temperature reached 102° at 2 P.M.

November 2. 200 fields were examined; 90 parasites were found—hyalin, 8; intracellular pigmented, 60; pre-segmenting, 22; segmenting parasites were specially looked for, but none found.

November 3. 200 fields were examined; 49 parasites were found—hyaline, 22; intracellular pigmented, 10; pre-segmenting, 16; segmenting, 1. On this day the chill occurred, with a temperature of 104°.

November 4. 200 fields were examined; 288 parasites were found—hyaline, 20; intracellular pigmented, 264; segmenting, 4. Temperature was 102° at the time of observation, but no chill occurred.

November 5 (last chill day). 200 fields were examined; 236 parasites were found—hyaline, 188; intracellular pigmented, 32; segmenting, 16. Injection was given on this day. No further chill occurred, and the number of parasites steadily diminished until finally they disappeared.

The accompanying charts, for which I am indebted to Drs. Robinson and Moore, internes at the Philadelphia Hospital, exhibit the decrease, disappearance, and return of parasites in this case and the temperature curves indicative of periodicity and freedom preceding and following the injection of the drug (Charts I, II, III).

One other case—that of quartan fever, being the only example of its kind in the series—may be cited in brief summary. It shows a period of freedom of twelve days and nine hours, interrupted by abortive disturbances on the intermediate days of paroxysm, and an apparent tendency to alternate periodicities of seventy-eight and eighty-four hours respectively. Whether the twenty-one-hour and forty-two-hour disturbances noted may not have some relation with quotidian and tertian periodicities, and what are the possibilities of a multiple infection, or of changes of type in organisms, are questions suggested by the case, but not answered (Chart IV).

Cosmo di G., aged twenty-three years, a native of Italy, by occupation a laborer, came into the hospital on June 17, 1907, with a history of having had an attack of chills and fever in Italy four years earlier, the paroxysms, according to the patient's statement, recurring after intervals slightly in excess of three days. The duration of this attack was three weeks, and the patient, although he suffered from irregular fever on various occasions thereafter, had had no second attack. The present illness began about five weeks before admission to the hospital, with a violent chill, which lasted about three hours and was followed by fever and sweating. Later, severe muscular pains developed, with extreme tenderness, especially of the trunk and abdomen. This was followed by the appearance of what, from the patient's description, seems to have been a maculopapular eruption, lasting about one day. According to the patient's statement, these paroxysms recurred every third day, and were followed by a like eruption. He had been given some pills, presumably quinine sulphate, but had not recovered.

Physical examination of the patient upon admission revealed nothing significant, other than slight enlargement and tenderness of the spleen. Irregularly distributed over the trunk and abdomen was a papulo-œdematous eruption, consisting of central spots of a pinkish color, surrounded by a purplish areola. This gradually faded, reappearing with high temperature paroxysms. After treatment was begun it disappeared altogether. The temperature upon admission was 101.3° at 5 P.M., June 17. Chart IV shows the course of the temperature during the patient's stay in the ward. Previous to the injection of 1 gram of quinine and urea hydrochloride, three periods of maximum temperature (about 103° F.) were noted,

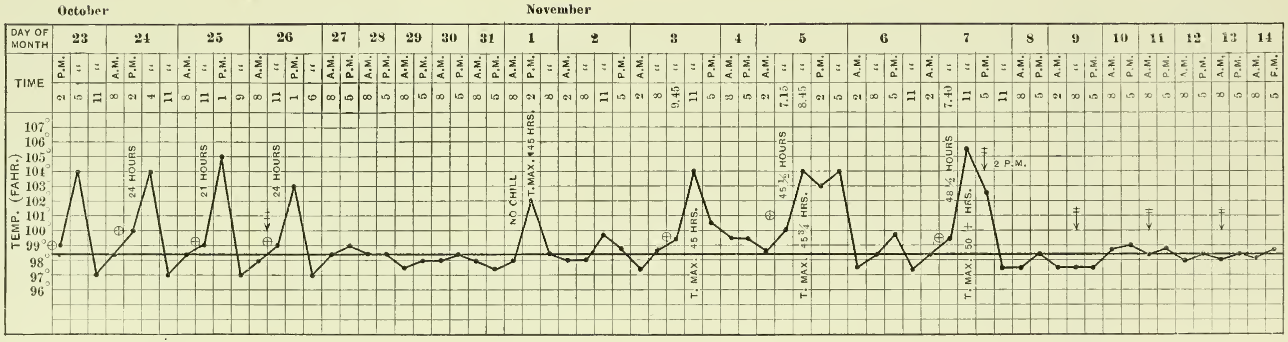

Chart I.—Quotidian intermittent fever. Free period 147 hours. Change of type to tertian. (Henry J.; Autumn, 1907.)

⊕ Beginning of chill. ↓ Injection of 1 gram of quinine and urea hydrochloride.

the intervals being, respectively, eighty-four hours and seventy-eight hours. Periods of minimum temperature (about 97° F.) followed the maximum temperature after intervals of, respectively, twenty-four, thirty-six, and twenty-four hours. Each of the periods of maximum temperature was preceded by a chilly sensation and followed by sweating. The decline of temperature to the normal point, or just above, occurred in from three to twelve hours, without medication.

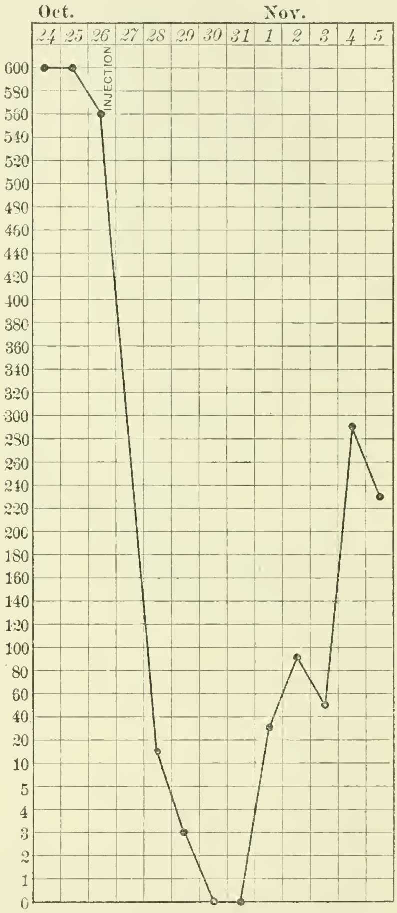

Chart II.—Showing disappearance and reappearance of organisms after the injection of 1 gram of quinine and urea hydrochloride. (Case of H. J.)

The blood on the day following admission showed: hemoglobin, 100 per cent.; erythrocytes, 5,104,000; leukocytes, 13,800—polymorphoneuclear, 73 per cent.; small lymphocytes, 13 per cent.; large lymphocytes, 13 per cent.; eosinophiles, 1 per cent. No organisms were found in several slides prepared from the fresh blood, nor were they discovered either in stained or unstained specimens until the 26th, when intracorpuscular forms were seen. On the 28th, the day on which the paroxysm, if quartan, was again due, both intracorpuscular and extracorpuscular forms were identified as the quartan parasite.

On June 28, at 6 A.M., six hours in advance of the paroxysm anticipated on that day, which was apparently due to occur eighty-four hours after the preceding paroxysm, the injection was given, the temperature at that time being 99.4°. No chilliness was felt, but the temperature rose 4 points to 99.8° F., about 3° less than the preceding maximum point and 4° less than the paroxysm with which its period of eighty-four hours apparently related it. No further injection being given, a period of temperature rise (100°) manifested seventy-eight hours later, another rise, again after seventy-eight hours, another twenty-one hours later, and another forty-two hours later. The patient complained of nothing. There was neither chilly sensation nor what might be considered marked rise of temperature until July 10, at 9 P.M., seventy-eight hours after the rise of temperature

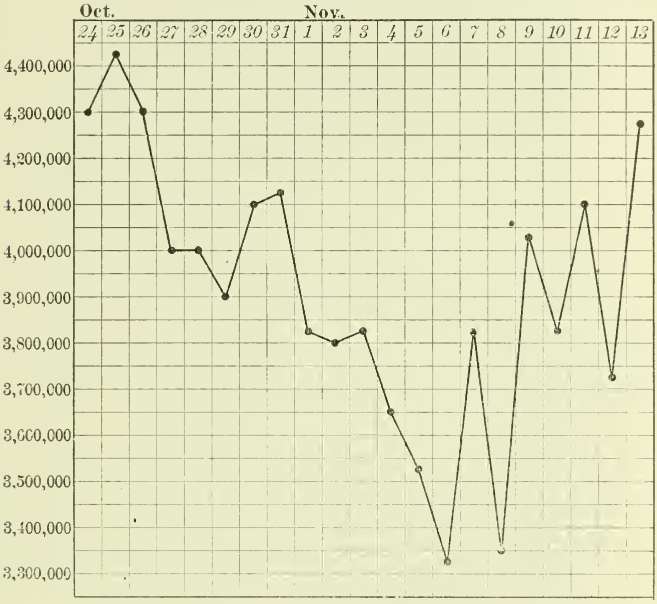

CHART III.—Erythrocyte count diminished after injection of quinine and urea hydrochloride (October 26), until disappearance of recrudescent organisms; then increasing interruptedly. The leukocytes varied during this period from 4600 to 4000, falling to the latter number on October 28, when the temperature became normal following the injection, and the parasites were only 12; they gradually rose, with remissions in count up to 4400 on November 5, when the temperature was 104.2°, and the number of parasites was 236. (Case of H. J.)

last noted, two hundred and ninety-seven hours (twelve days and nine hours) after the abortive temperature rise following the injection, and three hundred and eighty-one hours after the last preceding definite paroxysm. The next paroxysm, with a temperature rise to 101°, occurred July 14, at 9 A.M., the interval being eighty-four hours. This paroxysm shows a double crest, the second rise occurring six hours later than the first. Following this, injections were given at such intervals as to control the paroxysms and

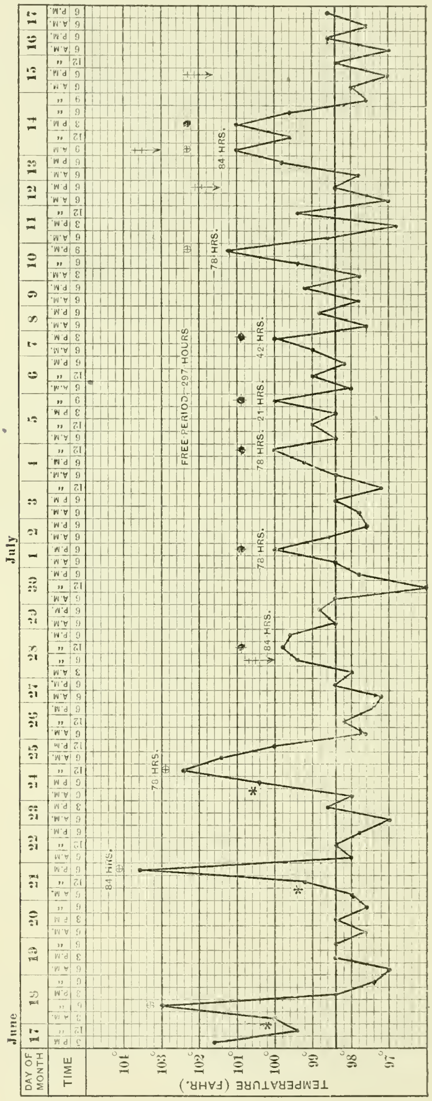

CHART IV.—Quartan intermittent fever. Free period 297 hours. (Cosmo di G.; Summer, 1907.)

* Beginning of chill.
⊕ End of chill.
⊕ T rise without chill.
■ Double crest temperature rise.
↑ Injection of 1 gram of quinine and urea hydrochloride.

assure recovery from the acute attack. Treatment appropriate to chronic malarial infection was then instituted.

During the period of observation the following notes were made concerning organisms:

June 26. Malarial organisms found—intracorpuscular forms.

June 27. Malarial organisms found.

June 28. Organisms—quartan—found. Injection given.

June 29. Coarsely granular bodies—intracellular, peripherally located. A few hyaline bodies found.

June 30. Extracorpuscular and intracorpuscular bodies found. The intracellular bodies were oval in shape.

July 1. None found.

July 2. Intracellular bodies, with coarse pigment, sluggishly motile; extracellular pigmented bodies.

July 3. Same as above, pigment more peripheral.

July 4. Same as above.

July 5. Nothing found.

July 6. Nothing found.

July 7. Nothing found.

July 8. Motile bodies (intracellular) found.

July 9. Motile bodies (intracellular) found

July 10. Temperature rise. Intracorpuscular forms and extracellular motile bodies found.

July 11. Intracorpuscular forms and extracellular motile bodies found.

July 12. No parasites found.

July 13. Parasites found, pre-segmenting forms.

July 14. Paroxysm. Injection given. A few parasites.

July 15. None found.

July 18. None found.

July 30. None found.

Temperature charts are also shown of a number of cases taken at random (Charts V, VI, VII). It will be observed that in one of these quinine chlorhydrosulphate was used instead of the urea salt and was in this instance efficacious. Other observations were made with it. While therapeutically active, it did not prove so uniformly dependable as the urea salt in the matter of the definite freedom period. Drawings of parasites observed were made in 1892, by Dr. Claribel Cone, then interne at the Philadelphia Hospital and now professor of pathology in the Woman's Medical College of Baltimore, to whom I am also indebted for careful notes of the cases which were under her immediate care.

Chronic Malarial Infections.—In chronic malarial infections of long standing, especially in those cases which exhibit considerable enlargement of the spleen or liver, or both, with or without marked alterations of the blood, quinine alone, even in the form of the combination with urea, has not been sufficient to bring about recovery. The quinine and urea salt, however, has seemed more efficacious than other preparations of cinchona and its alkaloids, with the exception of cinchonidine salicylate, and in no case has treatment without quinine been so satisfactory as when quinine has been used in conjunction, at various times, with salicin, methylthionin hydrochloride, arsenic, iodine, iron, and radiotherapy.

In those cases of chronic malaria in which there is a tendency to recurrence of acute exacerbations, whether manifesting as chills and fever or as gastric or nervous disturbances, the quinine and urea hydrochloride has been of distinct advantage in two ways: (1) When the recurrence is periodic, or assumes, after its initiation, a periodic type, quinine and urea hydrochloride used hypodermically or by the mouth, in appropriate dosage, and at a suitable time, will cause the acute symptoms to disappear promptly. For the remedy of the underlying cachexia or chronic affection, other means are additionally necessary.[3] (2) In cases in which the symptoms are irregular the injection of a small dose of quinine and urea hydrochloride will frequently bring about some definite order, either in the quality or time of the symptoms; after which they can be dealt with in the same manner as cases spontaneously definite and periodic.

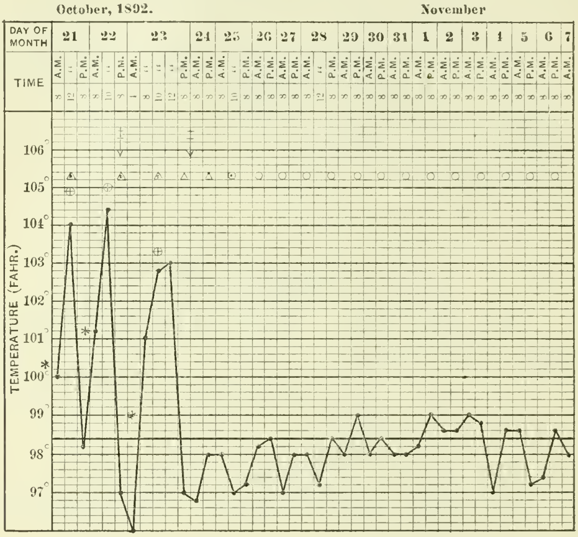

Chart V.—Quotidian intermittent of 30 days' duration prior to treatment. Two injections. Recovery. (John S.; Autumn, 1892.)

* Beginning of chill. ⊕ End of chill.

‡ Injection of 1 gram quinine and urea hydrochloride.

◬ Organisms, pigmented, numerous.

△ Organisms, pigmented, few.

⊙ Organisms, hyaline, few

o No organisms.

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[3] See also the author's articles in "The Polyclinic," Philadelphia, February 15, 1884, and January 15, 1886; and "The Philadelphia Polyclinic," March 15, 1893, and September 3, 1898.

In addition, the diagnosis is frequently made clear by the appearance in the peripheral blood of hemamœbæ, sometimes of atypical character, but still recognizable as varieties of the malarial parasite. This phenomenon will be spoken of more particularly in the next division of the subject, which concerns diagnosis.

Diagnosis.—In two ways has the hypodermic use of the double hydrochloride of quinine and urea proved useful in diagnosis.

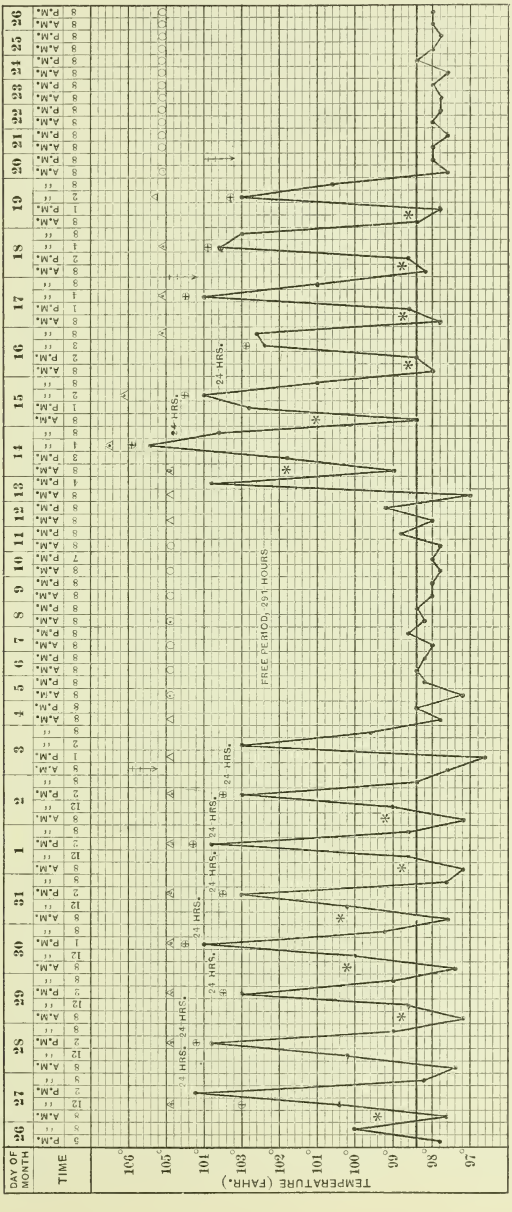

Chart VI.—Quotidian intermittent. Free period 291 hours. (Jos. D.: Autumn, 1892.)

* Beginning of chill. ⊕ End of chill.

‡ Injection of quinine and urea hydrochloride. △ Organisms, pigmented, numerous.

◁ Organisms, pigmented, few. ○ No organisms ⊙ Organisms, hyaline, few.

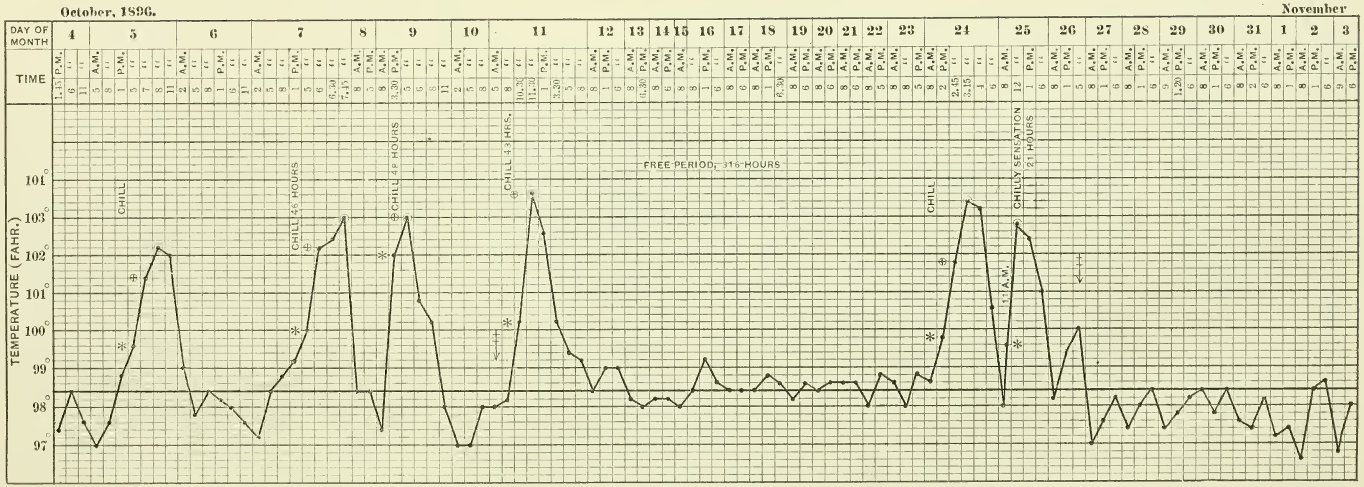

Chart VII.—Tertian intermittent. Free period 316 hours. (A. B. C.: Autumn, 1896.)
* Beginning of chill. ⊕ End of chill.
† Injection of 1 gram of quinine chlorhydrosulphate.

1. There are certain cases, evidently of acute infection, which resemble malarial fevers in the character or periodicity of the paroxysms, but in which malarial organisms cannot be found in the blood. There are certain other cases in which, despite the aberrant nature of the paroxysms, there is reason to suspect a malarial origin or complication, and in which, nevertheless, malarial hemamœbae have not been discovered. In nearly every instance of either of these groups the presence or absence of malarial infection can be predicated upon the patient's reaction to a single injection of the urea and quinine salt. The prolonged freedom period having been found to occur invariably in every case in which the organisms had been demonstrated, it is reasonable to assume that its occurrence indicates the dependence of the symptoms upon undiscovered, perhaps deep-dwelling parasites, and that its absence means the absence of malarial infection.

Thus, in the course of the earlier observations at the Philadelphia Hospital, at a time when 5 cases of intermittent fever of definitely proved malarial origin were under treatment, and manifesting, some the six and one-half days, and others the thirteen days, freedom period, there was a sixth patient who exhibited what appeared to be a typical temperature curve of quotidian intermittent fever, but in whose blood malarial organisms could not be demonstrated. He received a diagnostic injection of 15 grains of quinine and urea hydrochloride, which induced merely a temporary fall of temperature. Renewed questioning then elicited from the patient what had theretofore been denied, namely, a history of syphilitic infection some six months previously; and recovery promptly followed the use of mercurial inunctions.

In cases of typhoid fever, in which the temperature has tended to assume, at some period of the case, an intermittent type, but in which malarial organisms have not been found in the peripheral blood, diagnostic injections have, in some instances, been followed by the freedom period and in others have not so been followed. In these instances, and especially among soldiers of the Cuban war, observed in the months of July, August, and September, 1898 (Chart VIII), it was found that the freedom period usually occurred in patients whose marked loss of hemoglobin would in any event have raised suspicion as to malarial complication, that is to say, of double infection—malaria and typhoid. In some of those in whom the quinine treatment was not continued, because it did not seem to be clinically necessary, the malarial organisms made their appearance during convalescence, after the typhoid infection had run its course. In others, the continuance of the quinine treatment presumably prevented such definite demonstration of the diagnosis. In those cases in which a single injection of the quinine and urea salt had a temporary antipyretic effect, but was not followed by a prolonged freedom period, malarial organisms did not make their appearance so long as the patients remained under observation; and it is fair to conclude that in these cases that form of infection was absent.

2. The other method in which the injection of the quinine and urea salt has proved useful diagnostically has already been referred to in speaking of the treatment of chronic malarial infection. It was suggested to me by an old observation of Archibald Billings.[4] In cases of doubtful diagnosis the injection of a quantity of the drug not sufficient to secure a definite freedom period will frequently cause the appearance in the peripheral blood of organisms recognizable as normal or atypical forms of the hemamœba of malaria, and this has been observed so frequently and in so many diverse conditions that I am inclined to look upon its absence after, say, half a dozen injections, varying from three days to a week apart, and in doses increasing from 0.3 to 1 gram, as virtually excluding malarial infection. A typical instance of the value of this use of the quinine and urea salt is the case of chronic malarial infection with splenomegaly and blood changes resembling those of Banti's disease,[5] studied in conjunction with Dr. R. C. Rosenberger and presented to the College of Physicians of Philadelphia, in March, 1904. I am of the opinion that in such cases the organism is resting in some larval form—if the expression be appropriate—probably in the spleen or bone marrow, and that its appearance peripherally is part of a defensive, reproductive reaction to the paratoxic effect of quinine. That organisms do remain latent for long periods is well known; and I have elsewhere referred to a case in which they had reappeared annually for twenty years, provoking, usually, a gastric crisis. This phase of the subject, also, I hope some competent investigator will look into.

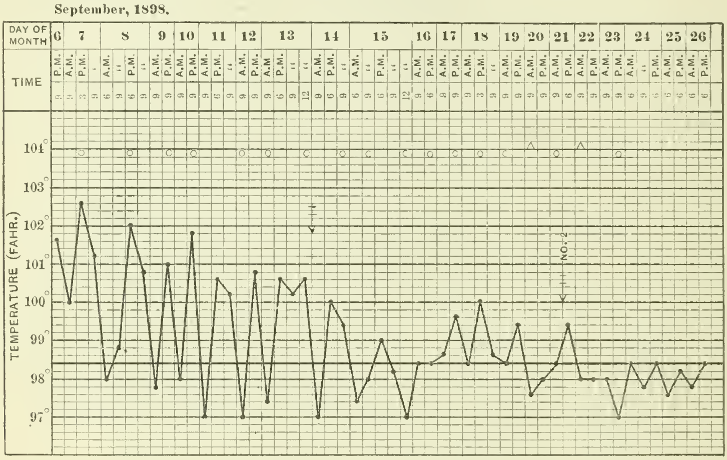

CHART VIII. (Illustrating diagnosis).—Mixed infection; typhoid and malaria. Widal reaction positive. Rose spots. (X. Y Z.; from Tampa, Fla.)

‡ Quinine and urea hydrochloride injected. ○ No organisms found.

△ Organisms found.

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[4] A. Billings, First Principles of Medicine, London, 1838, p. 218.

[5] AMER. JOUR. MED. SCI., August, 1904; Trans. Coll. Phys. Phila., 1904; Phila. Hosp. Reports, 1905.

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LIST OF THE CUTANEOUS AFFECTIONS OBSERVED IN ANGOLA, WEST AFRICA.

By F. Creighton Wellmann, M. D., Benguella, West Africa.

Having been invited by the Editor of the American Journal of Dermatology to contribute a paper on the cutaneous diseases seen in Portuguese West Africa, I have thought that the most useful form of preliminary communication would be a more or less comprehensive review of the subject as a whole. Such a plan of course excludes detail discussion of particular points, but I shall hope to present fuller studies of the more interesting and important affections on some future occasion There are several viewpoints from which such a study as the one proposed may be approached. The method adopted is to divide the diseases observed into several groups, largely defined by what seem to me to be the most probable views regarding their etiology, and largely to limit the remarks on them to special features not usually seen in practice at home. I need hardly say that any attempted etiological classification of tropical skin diseases is imperfect and tentative, but the same objection holds for a clinical, or indeed any other classification, and the plan followed possesses several advantages, not the least of which is that, writing as a pathologist pure and simple, I am enabled to omit many observations and details (including all the minutæ of treatment), which, if incorporated, would make the paper of unwieldly length. Most of the remarks have in mind the Umbundu-speaking Bantu natives of Angola. As I have already published a short description of these same people I shall not repeat it here. I have mentioned no diseases which I have not seen in the district studied. I have taken a liberal view of the scope of the article. And have perhaps included several affections not strictly within the domain of dermatology.

I. AFFECTIONS OF UNCERTAIN NATURE.

1. Hypertrophies.

(a) Warts, Cutaneous Horns, etc.—Warts are common enough and cutaneous horns are not seldom seem. Neither are, however, to be considered as precancerous states of the skin, since malignant disease, as I have elsewhere shown, is rare over all and almost unknown over considerable parts of the district studied. I have never seen extensive hyperkeratoses such as icthyosis, Darier's disease, etc.

(b) Keloids, Multiple Nodules, etc.—The first of these affections is, as is well known, amazingly common among the aboriginal natives of Africa, they seeming to have a peculiar fibrogenetic tendency. Scars from burns, tattoo marks, etc., often take on this character, and they are even intentionally produced for purposes of ornamentation. Cases of multiple painful subcutaneous tubercles are also met, as well as is *Molluscum fibrosum.* It seems to me that terms like *"Dermatitis nodosa tropica,"* etc., are premature and likely to be misleading through their probable inclusion of several undifferentiated affections under one name.

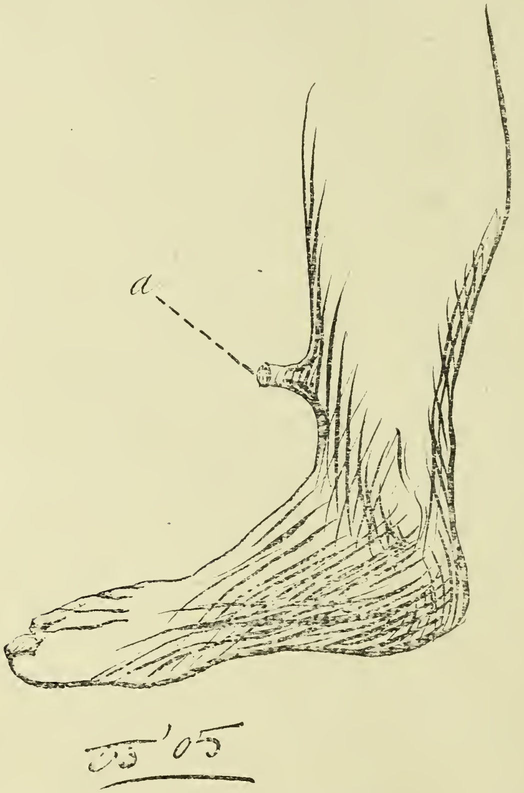

FIG. 1. Leg of Bantu woman showing cutaneous horn (a) on the shin.

(c) Gundu and Other Superficial Exostoses—While these do not, strictly speaking, concern the dermatologist, I follow Plehn in mentioning them in connection with cutaneous growth. Gundu, here called Uluyue, is occasionally seen. Small growths on various superficial bones, notably of the head and shins are also encountered.

2. ATROPHIES.

Very rare. Have seen a few cases of senile atrophy of the skin. Have never seen *Striae atrophicae.*

3. Dystrophies.

(a) Albinism, Leucoderma, Alopecia, etc. —Albinism, both partial and complete, is not rare. A striking affection designated by the natives "Uyamba," results in a curious blotching of the body that suggests pinta. I have, however, considered the disease to be a form of leucoderma, as the patches are always of one color, there is no itching, little desquamation, and mycelial filament are not found in the scales. The pigment changes, too, are slighter than in pinta. The Angola Bantus are not hairy, and have scanty beards. I have failed to find, however, but one case of genuine alopecia.

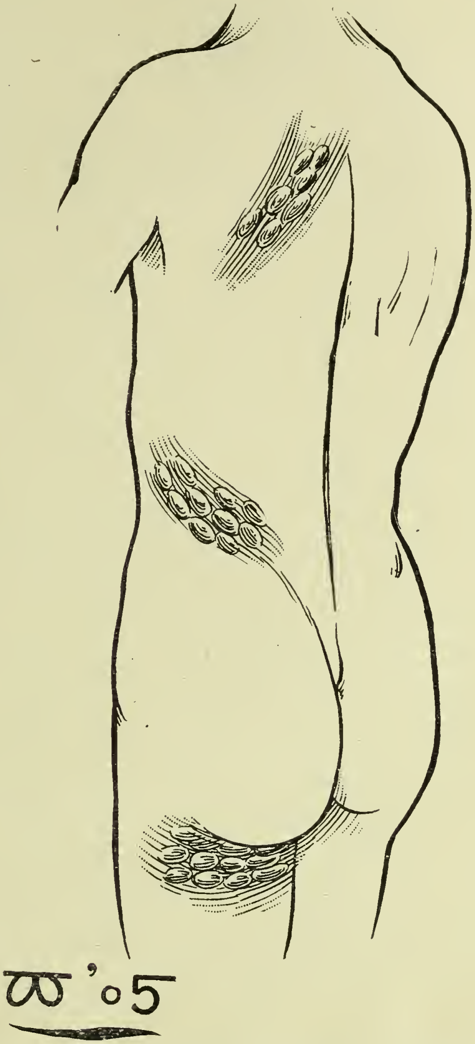

Fig. 2. Peculiar keloidal formations probably resulting from old scarification wounds.

(b) Unusual Coloring.—Defects in the color of the hair are sometimes seen. A common variation is a strong reddish tinge. Simple hyperpigmentation including the conjunctive and other unusual parts of the body is often noticeable.

4. Neuroses, Etc.

(a) Akatama.—This is a disease of which I have published descriptions on several occasions. Its character is sufficiently indicated in the name which I have given to it—*Neuritis peripheralis endemica.* It is characterized by

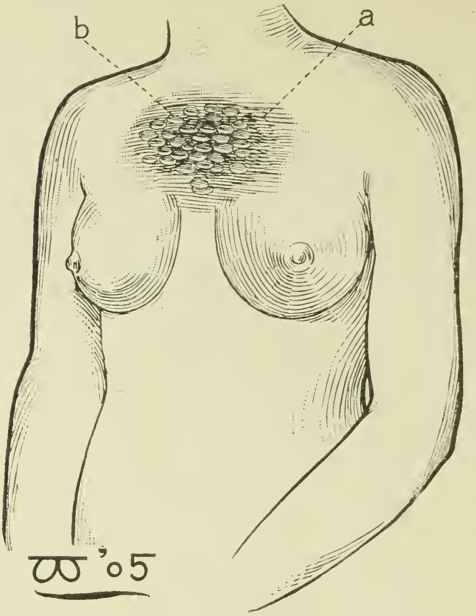

Fig. 3. Nodular keloids resulting from dermatitis set up by a native blistering mixture. (a) Zone of hyperpigmentation; (b) nodules.

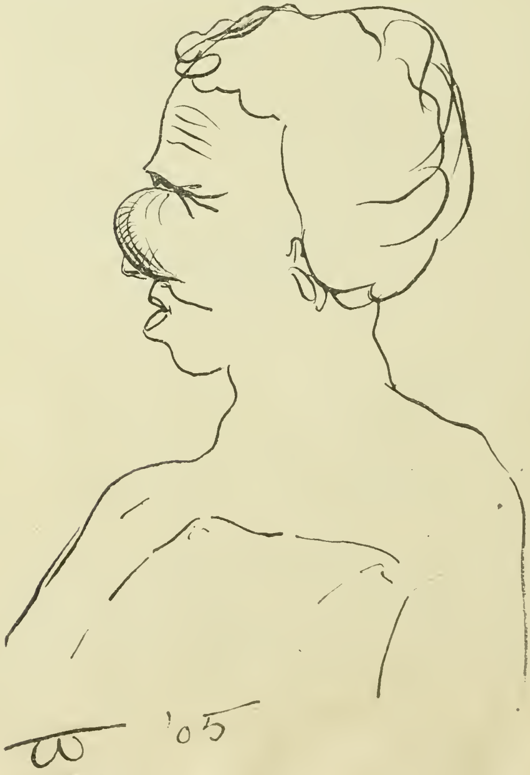

Fig. 4. Bantu woman with very large growth of "Uluyue" (Gundu).

numbness, pricking, burning, excessive sweating and slight edema of the skin, usually of the extremities. It is to be differentiated from acrodynia, and the various similar symptoms occurring in beri-beri, malaria, Strachan's disease, Reynolds' disease, etc., etc.

(b) Urticaria is common, often occurring temporarily after the bites of insects, etc. There are also other transitory edemas, itchings and eruptions which may be nervous in character.

II. CONDITIONS CAUSED BY PHYSICAL OR CHEMICAL AGENCIES.

1. Affections Due to Extreme Heat and the Sun's Rays.

As would be expected, affections of this class are almost entirely confined to the white population. Among others may be mentioned the following:

(a) Tropical Mask.—This is an abnormal deposit of pigment in the skin of the face, giving the subject something of the appearance of one suffering from Addison's disease. It is often accompanied by excessive wrinkling and harshness of the skin, probably to be traced to several causes obtaining in the tropics, and not to light and heat alone.

(b) Relaxed Sensitive Skin.—High temperature and the resulting constant perspiration often unite in bringing about a relaxed condition of the skin which greatly lowers its efficiency as a protective and excretory organ. In such persons constant care is needed to protect them from the always disastrous effects of sudden chill; and they are especially liable to vague eruptions, veldt sores, etc., etc.

(c) Solar Erythema.—Blondes, especially, suffer frequently from sunburn. The damage to the skin is sometimes extensive and severe.

(d) Prickly Heat.—Whether this and similar affections be due to excessive perspiration, an organism of low virulence, or what not, there is little doubt but that the continued high temperature is to blame in the first instance. In some subjects life on the coast is made almost unendurable by the disease.

(e) Dysiderosis.—One case which I saw resembling prickly heat, except that it was confined to the hands, would, I suppose, fall under the head of dysiderosis or cheiro-pompholyx.

2. Conditions Induced by Poisonous Substances.

A long list of small troubles could be furnished under this category.

(a) Poisonous Plants.—Of interest to the dermatologist is the severe irritation caused by touching certain plants, the fruit or leaves of which are clothed with minute poisonous hairs which come off and remain sticking in the skin. Two of the commonest of these plants are *Leguminosae,* one being *Mucuna prurieno,* D. C., which is called by the blacks "Eyumbi." The other, which I have not yet determined, is a vine called in the native tongue, "Sakupolopolo."

(b) Animal Substances.—Among animals a gastropod and a millipede are both capable of causing severe inflammation of the skin by crawling over the body. In the case of the former I have seen painful denudation of epidermis as a result of its acrid secretion, and the track of the latter over the skin looks as though a red-hot poker had been drawn across the body. I do not know of any mineral substance used by the natives which is irritating or otherwise injurious to the skin.

III. AFFECTIONS DUE TO VEGETABLE ORGANISMS.

1. Diseases Caused by Bacteria.

(a) "Veldt Sore," Ulcers, Tropical Phagedæna, etc.—The typical "Veldt Sore," or "Natal Sore," is not seldom seen. The work of Herman seems to prove that the cause is a siplococcus (Micrococcus vesicans.*) Ulcers of various kinds, indolent, granulating and phagedænic, are very common. The so-called tropical sloughing phagedæna is worthy of special remark. Elsewhere I have written of it as follows: "I recognize two distinct forms of the disease—a severe and a mild—which I have called Rapid and Sub-acute Phagedæna. Rapid Phagedæna is a terrible affection, pursuing a relentless course through skin, soft tissues and even bone with frightful rapidity. Joints are disorganized in a few days, or even hours, and a limb may become a putrid mass in an almost incredibly short period. It is fortunately rare. I have seen it once beginning on the cheek. Treatment is of no avail." The attempt of Le Dantec to identify Tropical Phagedæna with the hospital gangrene of temperate climates can hardly stand in view of the remarkable readiness and thoroughness with which operation wounds heal in the tropics, and especially among blacks. I have never seen phagedæna, or anything resembling it, set up in operation wounds, even those made by native doctors with septic instruments. In regard to the sub-acute variety I quote again from the same paper: "It is that usually described in text books and is sharply differentiated from the above by its tendency to spontaneously arrest its course and set up granulations. Even in its initial stage it is milder and slower than the preceding (although quite severe enough), and recovery is the rule." I include the above ulcers in the present etiological group in deference to the opinions of several authorities. For instance, Mac Leod of the London School of Tropical Medicine said at the last meeting of the British Medical Association: "The phagedænic ulcer of warm countries is probably due to an undetermined form of bacterium." The Indolent Ulcer also deserves mention here. I quote once more from my paper above mentioned: "The frankly indolent ulcers are often of this type almost from the beginning of their course. They may be active for a few days only at the commencement, and all angry symptoms subside while the sore is not larger than a shilling-piece. It is this form which oftenest gives the history of dating from a spontaneous vesicle (*Vide* my note in the *Journal of Tropical Medicine* for April 15, 1905, p. 118), which was mentioned in connection with tropical ulcers by Bechtinger as far back as 1869. They may run on for years. I have seen them completely encircle a limb, although as a rule a 'bridge' of sound skin is left free even in severe cases. A good many ultimately recover, especially if kept clean." The following experiment (mentioned in the note alluded to in the preceding quotation) throws light on the etiology of such conditions: "Applicants for treatment who came with these ulcers last mentioned, generally described them as commencing in the shape of a blister 'which came of itself.' And some time ago a Bantu boy, whose sister had one of the ulcers under discussion on her leg, came to the dispensary with a large bleb on his cheek, another smaller one on the elbow, and a third on the inner surface of the leg just above the ankle. The natives

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*This is probably identical with *M. campaneus* described by Ogston.

†I have lately published a clinical classification of the principal tropical ulcers found here. Its outline is as follows:

1. Tropical Phagedæna.
    - (a) Rapid.
    - (b) Sub acute.
2. *Indolent Ulcers.*
3. Malarial Sores.

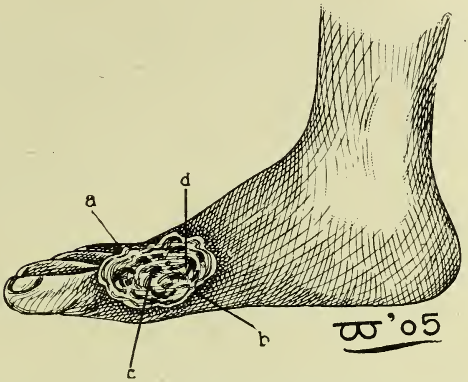

FIG. 5. Sub-acute tropical phagedaena involving the dorsum of the foot; (a) and (b) edge of skin and subcutaneous tissue; (c) sloughs; (d) granulatlons.

about all assured me that these blebs were the initial lesions from whence 'chronic sore' originated, saving that the ulcers follow only when the blisters appear on the lower limbs. I persuaded the boy to remain without treatment and in a few days the vesicles on the face and arm had disappeared (the one on the face, which I punctured for the purpose of examining its contained fluid, being the first to go), while the one on the leg had resulted in a small area of inflammation, the central portion of which was covered with a crust composed of inspissated serum, dirt, etc. On removing this crust a shallow ulcer was revealed which looked like other 'chronic' sores which I had seen in their early stage. The boy now refused to remain any longer without being treated, so the sore was swabbed with pure carbolic and an antiseptic dressing applied. It was healed at the end of a week. Fluid from the large bleb on the cheek (which was rather larger than a shilling piece) was seen under the microscope to be swarming with bacteria, which, on being sown in culture media proved to be staphylococci." The ulcerative processes which are probably traceable to bacterial infection of the skin, are common and of great importance, and I have accordingly devoted some space to an attempt at their differentiation.

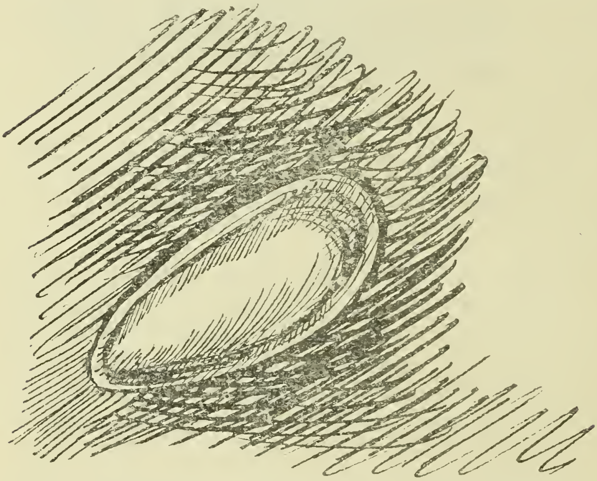

Fig. 6. Bleb from a peculiar case of pemphigus. Most of the blebs were of the form shown.

(b) "*Pemphigus contagiosus*" and Similar Affections.—There has been a tendency of late to identify the so-called *P. contagiosus* with *P. acutus* or *P. neonatorum* of temperate climates.

Manson speaks of finding a diplococcus in the epidermis and fluid of the blister. Various descriptions of Pemphigus-like conditions have been published from the tropics and there are probably several varieties. The form usually met by me in West Africa does not differ clinically from that often seen at home.

(c) *Granuloma pudendi.*—I have seen a few cases in women. I am inclined to agree with those who distinguish it from analogous conditions seen at home, and would further suggest testatively that it is due to a schizomycitis and that the granulomatous form taken on by the ulcers set up by its presence may, like keloids and similar manifestations, depend on some factor peculiar to dark races.

(d) "Ukau."—This disease is an eczema (*Eczema crustosum*) and is often very severe.

(e) Climatic Buboes.—I have recently made a study of 100 cases of these. From several I cultivated *Staphylococcus pyogenes aureus,* but have never succeeded in isolating anything resembling Kitasatos bacillus.

(f) Boils.—Rather rare. Differ in no wise from those seen at home.

2. DISEASES DUE TO STREPTOTHRICES.

I have never seen here an undoubted case of madura foot, which is becoming common enough on the East Coast. One case (which I did not have opportunity of examining closely) somewhat resembled mycetoma in its clinical features. I have not positively demonstrated the *Streptotricheae* in any cutaneous affection.

3. DISEASES DUE TO YEASTS.

A disease called by the natives "Ovilundu," and which they attribute to handling and eating a mushroom called by the same name as the disease*, may quite possibly be due to a Blastomycete. The macroscopical features of the disease somewhat resemble those of *Lupus vulgaris.*

4. DISEASES CAUSED BY MOULDS.

I have not seen *Tinea imbricata,* which is so common in the Far East. There are, however, several ringworms which deserve mention, but which I have not yet found time to properly study. Their differentiation would probably present considerable difficulty. The forms figured by Plehn from the Cameroons under the name "gemeinen tropenringwurms" are represented, and a small, very regular ringworm called "Ochindambi," which is usually confined to a single focus on the cheek or forhead, is also met. One affection usually spoken of as "Eczema" is a ringworm. A thorough study of the parasitic *Hyphomycetes* of hot climates is urgently needed.

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*Leucodermia, "Uyamba," and Eczema, "Ukau" (*Vide supra*), are also thought by the natives to be caused by eating and handling two species of mushrooms, also known respectively as "Uyamba" and "Ukau."

IV. AFFECTIONS CAUSED BY ANIMAL PARASITES.

1. Those Due to Protozoa.

(a) "Malarial Sores."—This type of sore usually appears as a small, definite, generally round, punched-out ulcer which I have called "malarial," because it as a rule heals quickly under the local application of quinine. The name, which I adopted from other writers, is not exactly fortunate, as the sores are quite possibly not all malarial in origin. This type would probably include certain lesions described by F. Plehn on the Tanga Coast and in other places. The ulcers are generally multiple and of comparatively trifling importance.

(b) Yaws.—I include frambæsia under affections due to protozoa, for the following reasons: On July 14, 1905, I found a spirochæte in the papules of a case of yaws. It could not be found in the patient's blood nor was I able to confirm my discovery in later cases. In the course of my regular communications to the American Society of Tropical Medicine I mentioned my find. I quote a paragraph from that communication: "Some time ago while examining a scraping from a yaw's papule I was somewhat surprised to see under the 1-12 inch homogeneous immersion lens several active spirilla-like bodies which in form and movement closely resembled *S. obermeieri.* Thinking it to be a case of the parasite of relapsing fever, I thereupon made a prolonged and careful examination of the blood, which, however, contained no spirochetæ. I found the parasites in other papules of the same case." Several weeks after my communication on the subject had been sent to America I received the report of the meeting of the British Medical Association, at which was read Castellani's paper announcing the demonstration of spirochetæ in the papules of two cases of yaws in Ceylon. As Castellani's observation was published before mine, the latter must now be regarded as a confirmation of his discovery (which has been spoken of as "one of the most important discoveries of recent times, considering the fact that the *Spirochaeta pallida* has been found by Schaudinn in syphilis and considering the relation said to exist between yaws and syphilis")*, but it is significant that the observation should have been almost simultaneously made in two such widely separated countries as Ceylon and West Africa. The natives believe there are two kinds of yaws, called by them "Ohumbula" and "Omunono," respectively. The one is supposed to be characterized by small and the other by large sores. The cases I have seen have been very typical. Considered by them a venereal disease. I know of one white man who acquired it.

2. Cutaneous Helminthiasis.

(a) Filiariasis.—While *F. perstans* is the usual form showing embryos in the circulation, yet other filariæ (*F. nocturna* and probably *F. diurna*) are also found, especially near the coast and elephantiasis (native name "Ovisonya") is not seldom seen. The legs are usually the part affected, but I have seen an enlarged scrotum weighing over fifty pounds. There is a growing disposition to throw doubt on the long-accepted etiological theory of Manson which I cannot better state than in the words of Mac Leod: "*Elephantiasis arabum* is attributed to the blocking of the lymph channels by the immature ova of the *Filaria bancrofti,* but this explanation is unsatisfactory. It would appear that some other unknown agent is at work in the production of elephantiasis. In Europe we are familiar with localized elephantiasis, believed to be due to streptococcic infection associated with recurrent attacks of local erysipelas, giving rise to permanent inflammatory changes in the affected tissues, the lymphatic obstruction being secondary to the vascular changes." I myself have seen a typical case of elephantiasis of the leg occurring in a man who had never been out of England. While it seems proven without doubt that elephantiasis is usually associated with filariasis it would seem to me to be quite in line with sound pathology to attribute some of the severe later inflammatory changes to secondary streptococcic or other bacterial infection such as occurs in diphtheria or (to take an analogous disease also caused by animal parasites) sleeping sickness.

(b) Uncinariasis of the Skin, and Invasion by Other Entozoa.—I have seen eruptions on the lower limbs which correspond to those caused by the penetration of the skin by the rhabdite larvæ of *U. duodenalis,* and on one occasion observed an entozoal embryo in the blood stream, concerning which I have written as follows: "In my last report on the disease incidence of my district in West Africa I figured and described an unknown entozoal embryo found in the blood stream of a young negress. It was different from the so-called *Anguillula stercoralis* and from the embryo of *Uncinaria duodenalis.* Its presence in the circulation puzzled me, although I referred at the time to Looss' work with larvæ of *U. duodenalis* as indicating a possible explanation of the presence in the blood of the worm seen by me. My exact words on this point were as follows: 'That the embryos of at least some entozoa can pierce the tissues of their host is proven by the experiments of Prof. Looss with the embryos of *A. duodenale* in Egypt, some of whose preparations I have seen. Bentley's work on the etiology of Panighoo in Assam proves the same thing.' Later researches by Looss show that the larvæ after piercing the skin leave the subcutaneous tissue in the blood stream, and, passing through the right heart to the lungs, travel up the trachea and down the œsophagus to the stomach and intestines. These researches having been fully confirmed by the later work of Schaudinn, Smith, Lambinet, Herman, Boycott and others, it has occurred to me that my worm may be the larval form of some other intestinal parasite which when observed was in the process of reaching by a similar route its normal habitat in the alimentary canal." It may quite possibly prove to be the case that several obscure irritative conditions seen in the tropics are connected with helminthiasis of the skin.

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*Brit. Med. Jour., Aug. 5, 1905, p. 282.

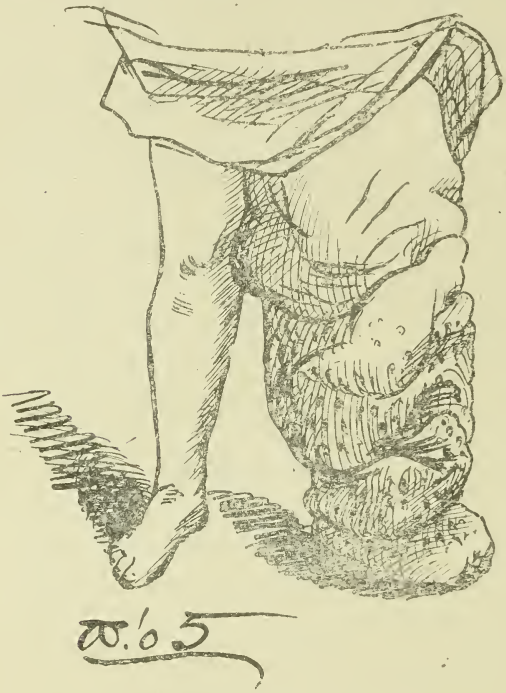

FIG. 7. Elephantiasis arabum.

3. AFFECTIONS DUE TO NOXIOUS ARTHROPODS.

(a) Arachnids.—(1) Scabies is common. The severity ranges from cases in which a few slight papules may be found to almost incredibly severe and neglected cases which may present all the symptoms enumerated in the descriptions of "Craw-Craw." I have failed to find filariæ in the papulas of "Craw-Craw," but the itch mite (*Sarcoptes scabei*) can almost always be demonstrated. In the worst cases large excoriations and ulcers are seen. "Craw-Craw" is a term which includes almost any sort of skin disease and should be dropped from scientific literature. Plehn's "*Dermatitis ulcerosa tropica*" is almost as unfortunate. An attempt should be made to differentiate these vague tropical ulcerative processes either etiologically or by more careful clinical study.

(2) *Demodex folliculorum.* Can occasionally be squeezed from the skin of the nose or forehead.

(3) Ixodiasis. Ticks are common and troublesome. Many insert the mandibles and toothed hypostome so firmly into the skin that if the tick is pulled off the head remains attached to the host. Others, like *Ornithodoras monubata*, do not fix themeslves to their host but bite at night and hide during the day like other vermin. The bites of several ticks cause swelling and irritation, which does not subside for days. The wheals are hard, raised and itch and swell most disagreeably when scratched even a week after being bitten.

(4) Bites of Spiders, etc. A tarantula and a large round-bodied spider which spins a golden web (*Nephila sp.*) both can cause severe local inflammation, edema or even sloughing of the skin by their bite. A pediphalp and a true scorpion (both called "Enyenya") are also greatly feared.

(b) Myriapods.—A millipede with poison in its feet has already been mentioned. Several large "centipedes" called "One," "Ochindundu," etc., set up by their bite severe irritation and local inflammation of the skin.

(c) Insects.—(1) Rynchota. *Pediculus capitis* and *P. vestimenti* are common and cause characteristic skin lesions, which are more marked in whites than in blacks. *Pthirius pubis* I have not seen. *Acanthia lectularia* is often met in native huts.

(2) Diptera. (a) The blood-sucking diptera of this region are quite peculiar to themselves, and my collections contain a number of flies new to science. The bites of some set up a very appreciable irritation of the skin. Among the most important of these may be mentioned the Tsetse fly of the district, *Glossina palpalis wellmani,* Aust., *sub-sp. nov.*, several species of *Stomoxys,* a number of new *Tabanidae* of the species *Tabanus, Haematopota* and *Chrysops,* one or two species of *Similium* and many mosquitoes, the most bloodthirsty and venomous of which are *Culicinae,* and some of which like *Culex hirsutipalpis, Danielsia wellmani, Mansonia uniformis, Heptaphlebomyia simplex* and various *Stegomyiae,* occur in great numbers and become of interest to the dermatologist from the irritation and even inflammation of the skin due to their bites. Among fleas *Pulex irritans* and several other species parasitic on birds and mammals (one of them new) have been found. The chigger, *Sarcopsylla penetrans,* deserves special mention here, as its ravages not seldom result in extensive destruction of skin and subcutaneous tissue.

(b) Ainhum. This disease should probably be discussed in this connection. I have elsewhere given *in extenso* my reasons for rejecting the view that ainhum is in any way connected with leprosy, and have on several occasions pointed out that the chigger may play some part in the causation of the trouble. I extract here a paragraph bearing on this point from a former paper: "Some time ago while engaged in a study of the chigger (*S. penetrans*), and later during the observation of several cases of ainhum, I noticed that the chigger has, even in healthy feet, a predilection for the under surface of the little toe, and especially so if, as is so often the case, the skin is cut or torn. It is well known to those who have studied the habits of the chigger that the insect invades abraded or irritated surfaces oftener than sound skin. The fold of skin under the proximal joint of the little toe corresponding to the edge of the web between the toes is the point where wounds are oftenest made by the sharp grasses, etc. through which the barefooted native walks and runs. The principal reason for this in the African is that the little toe of barefooted negroes lies separate from the others at an angle due to anatomical reasons connected with flatfootedness. As I have said, chiggers are oftenest found on the under surface of this toe, even when all the toes are intact. When wounds are once made here, however, the chiggers persistently invade them, and must be removed constantly. While I do not wish to be read as advocating *S. penetrans* as the sole cause of ainhum, it seems to me that these insects must play a part (in some instances at least) in the continued irritation which, especially in blacks (who have a fibrogenetic tendency) may lead to the contracting fibroses occasionally resulting in the spontaneous amputations known as 'ainhum.'" It may be further stated that such a theory goes far to account for the geographical distribution of the disease, which is particularly common in the two great homes of the chigger, viz: tropical America and Africa.

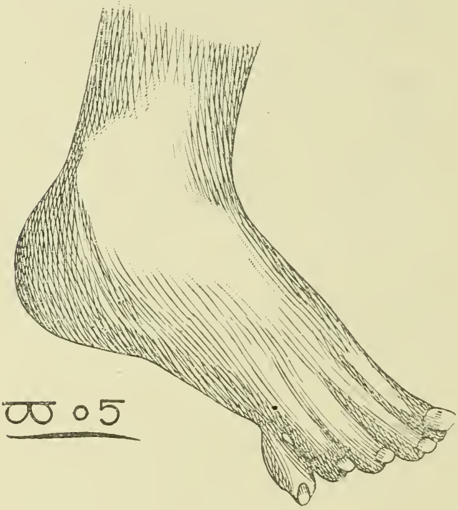

FIG. 8. Ainhum in its early stages.

(c) Myasis. Cutaneous myasis is not rare. I have seen and reported several cases. In some instances I have bred out the imagines from the larvæ. The flies in one case proved to be *Sarcophaga sp.* In another they were *Anthomyinae.* The curious blood-sucking larva of *Auchmeromyia luteola* should also be mentioned here. This maggot, as is well known, infests beds and sucks blood like lice, bedbugs, and other vermin. In a recent case of cutaneous myasis occurring in otherwise sound skin, however, I extracted a maggot identical (in size, shape, and, so far as I could see, every detail, including the curious mouth parts) with the usual hæmophagus larva of *A. luteola.* It would be an interesting instance of heterogenesis should these anomalous blood-eating maggots prove to be capable under certain circumstances (possibly when the skin is slightly broken from any cause) of producing, like their allies the larvæ of *A. depressa,* ordinary cutaneous myasis in addition to their equally disgusting *role* as vermin.

(3) Lepidoptera. The larvæ of several unknown lepidoptera are variously called "ochisia," "ochipia," etc., and are possessed of poisoned hairs which when touched remain in the skin and cause extraordinary irritation, characterized by itching, burning and transitory edema. Such caterpillars are carefully avoided by the natives.

(4) Coleoptera. One or two beetles possess the power of slightly irritating the skin.

(5) Hymenoptera. Wasps, ants and bees deserve mention. The stings of wasps are oftentimes severe and produce swelling, pain and occasionally urticaria. Several ants are poisonous. One has a sting which is said to be as severe as the bite of many poisonous snakes. Another secretes a violent venom resembling pus in appearance from glands at the roots of its mandibles. A third ejects a very acrid substance from the posterior part of the abdomen. Space forbids the review of other interesting details concerning similar insects. I have not yet heard from 166 species of noxious arthropods lately collected and forwarded to the British Museum.

(d) Vertebrates.—Of these the *Reptilia* are chiefly of interest in connection with the subject of this paper. The bite of several snakes, chief among which is the puff adder (*Clotho arietans*) sometimes gives rise among other symptoms to severe local and general eruptions, which latter are probably due to a remote selective action of the venom on the central nervous system.

In conclusion I may only advert to the cutaneous manifestations of several exanthematous diseases such as amaas (milkpox), chicken pox, etc., and of such general diseases as leprosy, syphilis etc. A very fatal disease not yet thoroughly studied is called by the blacks "onyalai," and is marked by the formation of peculiar hemorrhagic bullæ in the skin and mucous membranes. These and other questions must await another occasion for their discussion. The inclusion of even brief excerpts from my notes on various related topics which might fairly be treated in an article of this kind would have made a preliminary sketch like the present paper entirely too elaborate.

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THE LITTLE KNOWN ATYPICAL (UNFERTILIZED) EGG OF ASCARIS LUMBRICOIDES.

By O. T. Logan, M. D.,
Changteh, Hunan, China,
Medical Missionary.

Published under the Imprimatur of the American Society of Tropical Medicine.

My attention was called to this egg in 1903, having found it so frequently in the stools of patients, either alone or associated with the eggs of various other parasites we have so constantly in this region. In 1904, myself and another member of my family had this egg constantly in our stools, repeated examinations on different days showing it, unassociated with any other egg. I determined to play the part of investigator and subject and dislodge the worm if possible, so I took a full dose of santonin in tablet form and found in the stool next morning—the tablets! Powdered santonin gave results in the shape of a nine inch worm that differed only from the classical female *Ascaris lumbricoides* in that it had a constricting band at the junction of the middle and the anterior third of the body, corresponding to the genital orifice. No other worm was passed, and the eggs ceased.

In 1906 I published (1) the report of six cases, the patients being Europeans who were under my care, the fæces of whom all showed this peculiar egg unassociated with any other form. In all these cases but one, a single female worm was passed,

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after which the eggs ceased. The exceptional case was one in which two females were expelled. From a study of these cases, I was led to believe that we were dealing with unfertilized eggs and not those of a new species, as others and I had first thought.

During this time I had been in correspondence with Dr. Stiles, of Washington, who kindly examined specimens of worms sent by me. After the receipt of a batch of thirty or more worms, the total output of a Chinese who had been passing both typical and atypical eggs, he wrote me under date of October 8, 1906: "I have found the same peculiar ascaris egg in a patient in Washington, and looking up the literature I came across an article in the *Centralblatt für Bakteriologie und Parasitenkunde* in which the author refers to the peculiarity of certain eggs, and came to the same conclusion which

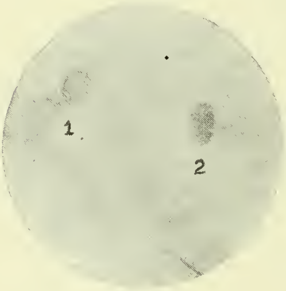

FIG. 1.

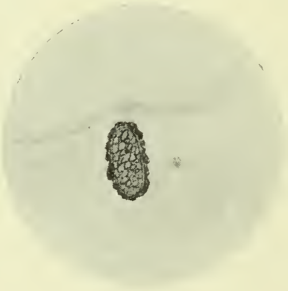

FIG. 2.

FIG. 1.—Photomicrograph of eggs of *Ascaris lumbricoides;* 1, fertilized egg; 2, unfertilized egg. x 100 (approximate).
FIG. 2.—Photomicrograph drawing of egg of *Ascaris lumbricoides*, unfertilized. x 500 (approximate).

you have reached, that they are not fertilized. I have studied quite carefully the tails of the two males which you forwarded. The papillæ seem to agree essentially with the papillæ described for *Ascaris lumbricoides* in Europe. I do not, therefore, feel justified in concluding that your specimens represent a new species, but am inclined to agree with you that some of the eggs you have found are unfertilized."

The peculiarity of the unfertilized egg is that, when taken from the uterus, it appears as a finely granular, elliptical mass enclosed in a very delicate membrane. The typical or fertilized egg taken from the uterus has the same thick shell that is found when the egg is found in the fæces. In the fæces the appearance of the unfertilized egg is so different from that of the same egg taken from the uterus that one who has not studied the matter thoroughly would not suspect that he was examining the same egg; for, instead of finding the yolk finely granular, it is found to be coarsely globular in the fæcal specimen. The albuminous coating of the unfertilized egg is much less in volume than the coating of the typical egg, and projects from the shell somewhat like blunt saw teeth.

Wellman (2), of Africa, who has studied the egg, both as taken from the uterus and as found in the fæces, concludes that the bile in the fæces stains the envelope of the egg in such a way as to mask the yolk.

The unfertilized egg is considerably longer and somewhat narrower than the fertilized egg, and is generally markedly elliptical with a tendency to flat-ten at one or both ends under pressure. Occasionally it is oval in shape, but never round.

This egg has caused much speculation by different observers in many parts of the world. Fleet Surgeon Beyer wrote me from Manila (3) that the egg had puzzled him. Maxwell (4), of South China, has been working at a solution of it for some time, as has Jefferys, of Shanghai, who writes me that he has tried to incubate the egg, but without success. Booth (5), of Hankow, a recent student in the London School of Tropical Medicine, wrote me that he was working on this egg, so it would seem that it is not well known in that school. Until recently, I have been unable to find a reference to the egg in any book on parasitology or clinical diagnosis in the English language. Hume, of Changsha, recently called my attention to a volume, an American publication, I am glad to say (6), that gives a very good description, with cuts and measurements, of this unfertilized egg.

My observations were made independently, and I do not know who should have the credit of priority in the matter. The purpose of this article is not to make claims, but to advertise the fact that such an egg as I have tried to describe is the constant product of the female *Ascaris lumbricoides* that fails to get her eggs fertilized.

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The Tropical Diseases of the Philippine Islands, With Especial Reference to Amebic Abscess of the Liver.*

By EDWARD WARWICK PINKHAM, M. D., of New York City.

Mr. Chairman and Gentlemen:—

I feel deeply the honor of being invited to speak a few words to you on tropical diseases as I found them. My remarks must of necessity be desultory and of a purely personal nature. My experience was gained in the Philippine Islands while serving for a period of about two years, as Assistant Surgeon in the regular army, and showed in a somewhat startling manner how unprepared we were both in our previous training and in our equipment to cope with the diseases peculiar to that region.

The diseases encountered with which we had not previously been familiar were the bubonic plague, beri-beri, dengue, sometimes not easily distinguished from malaria, tropical ulcer of the foot, the dhobic itch, and tropical or amebic dysentery. Cholera did not break out until after I was ordered home.

Of the bubonic plague I saw a little while I was in Manila. Those affected were nearly all natives or Chinamen, although I saw one case in a white man. It was that of a civilian teamster who fell from his wagon in a fit, and died four hours afterwards. His disease was demonstrated to be the plague.

Of beri-beri I saw many cases the greater part of them being natives or Chinamen. Two of our officers were afflicted with slight attacks. Had these two officers been in New York City at that time I should have made a diagnosis of multiple neuritis, perhaps alcoholic. We used to believe that beri-beri was caused by unhygienic living and surroundings. Cases did improve and some got well by change of environment. This was in 1900, and the rice theory came later.

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*Read at the Fourth Annual Meeting of the American Society of Tropical Medicine, at New York City, March 29, 1907, and printed under the imprimatur of the Society.

We encountered a good many types of fever which we were accustomed to diagnosticate as being either malaria or dengue. If the patients had pain in their bones and got well promptly we called the disease dengue. If they had a protracted fever or died we called the disease malarial whether the plasmodium was demonstrated or not.

The so-called tropical ulcers affected the feet and ankles. At first we believed them to be caused by ill fitting shoes or a lack of cleanliness. But even when care was taken with the shoes and feet, and bathing was insisted on, the ubiquitous ulcer persisted.

The dhobie itch, a form of tinea, was invariably laid to the washerwomen. Everybody, from the General down, was affected. One soldier in my regiment had the disease so violently that he looked like a tattooed man. The whole body, including extremities, scalp and pubes, was covered with the eruption. This man almost went insane from the itch. A supersaturated solution of salicylic acid, made by the addition of alcohol, was the successful remedy used.

Shortly after our regiment, the ninth infantry, landed, the soldiers began to be affected with diarrhea, with or without blood. They were immediately dosed with camphor and opium pills or subnitrate of bismuth. The most of them got well, but some of them were sent back to Manila with a diagnosis of bloody diarrhea, or dysentery. It was surprising to note the large number of soldiers so afflicted who never returned to duty.

Dysentery of the amebic type soon proved itself to be the scourge of our troops. At first we thought we could cure it by irrigation of the rectum and colon with a solution of quinin, and by the diet, but in this we found ourselves mistaken. It did not surprise us particularly to have patients die from exhaustion after frequent and profuse hemorrhages, but when they died three or four weeks after we supposed that they were cured of the dysentery we were extremely puzzled. Up to May, 1900, my experience had been with troops in the field. But at that time I was ordered to Iloilo, on the Island of Panay, for duty as operating surgeon at the second largest military hospital in the islands. It was here that I learned the key to the cause of some of the hitherto unexplained deaths which occurred during and after attacks of dysentery, namely liver abscess of the amebic type. In regard to this affliction I shall ask your indulgence while I quote from a paper on the subject written by me for the Society of Military Surgeons in 1904.

"Among the more serious cases admitted were those of tropical abscess of the liver, accompanying or following amebic dysentery. Sixteen of these cases came under the writer's care and were treated surgically." (Description of cases omitted.)

"In this series of sixteen cases there were seven recoveries and nine deaths. The percntage of mortality is very high, but it can be easily accounted for. In eight of the fatal cases an autopsy was made and revealed conditions which could not have been discovered beforehand, and which rendered a fatal result certain. In some of them the operation gave a measure of relief to the symptoms, but could do no more.

It may safely be assumed that without surgical attention all these patients would have died. In a few of the non-fatal cases a spontaneous discharge of the abscess might, under favorable circumstances, have occurred, leading to the recovery of the patient. But the circumstances in the Islands were not favorable; the patients were, almost without exception, emaciated and weak; the tendency of the dysentery was to recur and of the suppurative process to spread, making the chances of a spontaneous cure very small. It may, therefore, be rightly claimed that in this series of operations seven lives were saved and none sacrificed.

"Not more than six of these cases entered the surgical ward of the hospital with a correct diagnosis. In two of them the abscess was only suspected. In the other cases there was a wide range of diagnosis, embracing appendicitis, malaria (accounting for the chills), acute pleurisy, acute pneumonia, peritonitis, empyema, convalescence from typhoid fever, and delirium tremens with pain in the side. Gall stones, with or without cholecystitis, were apparently not thought of in this connection probably because the severe pain which usually accompanies this affection was absent.

"Abscess of the liver is a very rare affection in northern latitudes, and the literature of our ordinary books of reference is meager in regard to it; hence it is not strange that such very reasonable errors of diagnosis should be made by those who had had little or no experience in the treatment of tropical diseases. After a while the surgeons became more familiar with this common sequel of tropical dysentery so that they were on the lookout for it and made the diagnosis more readily. These errors in diagnosis, together with the total failure in all the cases to recognize the disease in its early stages account, in a large measure, for the high rate of mortality. A prompt recognition of the complication and appropriate treatment might have enabled us to make a different showing."

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"It is seen that in a majority of cases dysentery was a concomitant affection. In those cases where there was no dysentery recovery followed. In all the cases there were emaciation and debility, and these were prominent factors in the fatality, or rather in the production of conditions which rendered a fatal result more likely to happen. The loss of flesh and great weakness were due, of course, to the long drain upon the system both of the dysentery and of the unrecognized abscess, together with the depressing effects of the tropical climate.

"In thirty-two autopsies made on the bodies of those whose death had been ascribed to dysentery, abscess of the liver was found in five. In one case the liver was so filled with abscesses varying in size from the size of a pin's head to that of a pecan nut, that the cut surface of the right lobe gave the appearance of a "polka dot" piece of yellow brown cloth. A similar appearance was noted in one of the cases operated on.

"These so called abscesses of the liver are not true abscesses, nor are their contents pus. They are rather areas of necrosis, or liquifaction of the liver tissue, and their contents are made up of liver cells in all stages of degeneration and disintegration, free fat globules, more or less of blood corpuscles and serum. In this paper the terms abscess and pus are used for convenience. An examination such as was possible with our imperfect outfit, was made in all the cases of the contents of the abscesses. Amebæ were found in eight of the cases. In some of these they were not discovered until the scrapings of the abscess walls had been examined. In the cases of long standing single abscesses followed by recovery amebae were not found. In all the cases where there was concomitant dysentery amebae were found in the stools. In all cases except the first it was made a practice to curette the walls of the abscess before packing, the object being to remove as much of the infected tissue as possible. The scraping was done very carefully and with a sharp curette.

"Finding an abscess in these cases is often a matter of luck; for unless there is a localized swelling of the liver surface there is no way of locating the pus except by the aspirator, and this sometimes fails even in cases where an abscess is afterwards found on section.

"In making a diagnosis of abscess of the liver the previous history of the patient is of the utmost importance. If a patient gives a history of having had dysentery of a tropical, or amebic type, if he has an indefinite pain, or a sensitive feeling over the liver area manifested on compressing the ribs on the right side, the pain radiating to the right shoulder; if he has chills, or chilliness, and more or less of fever, similar to that of septic infection, abscess of the liver may be suspected, whether or not the liver shows signs of enlargement. When dysentery is coexistent with the symptoms above mentioned it is almost certain that an abscess exists. Aspiration may be an aid to the diagnosis, but it is by no means a certain one. The liver may be punctured a number of times without obtaining pus, and afterwards on operation an abscess may be found. It is a good plan, however, after a patient is anesthetized to aspirate, for if pus is found the needle is a good guide to its locality, and if it is not found no harm is done. Aspiration under cocain proved in one of my cases to be an unpleasant and indeed somewhat dangerous proceeding. It is not, in my opinion, to be advised in these cases, for as a rule the patient's condition is too poor to stand much of the depressing effect of the drug."

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"One interesting fact brought out by these operations is the demonstration of the freedom with which one may search through the liver tissue without dangerous hemorrhage. The search should be made by the finger rather than by any sharp or steel instrument. The finger seems to slip over the vessels without rupturing them Manson lays stress upon the danger from hemorrhage in exploring the liver and speaks of the great friability of the tissue, making it extremely difficult to sew the liver to the wound. Neither of these troubles did I experience to any great extent.

"It is my opinion that no abscess, whether bulging or not, should be evacuated and drained by means of the trocar and canula as suggested by Manson. There may be adhesions of the liver to the wall and there may not be. Most likely they do not exist. One cannot be sure in any case, and the risk is run of infecting the thoracic or abdominal cavity if this method is followed. The operation by incision is surer and safer, and the shock to the patient is not greater except in extreme cases, and in these the quickest method is the best.

"Osler, in an article in the *Medical News*, of April 12, 1902, speaks of a diffuse cyanosis, as present in cases of abscess of the liver. This symptom was present in so many of the poorly nourished soldiers suffering from a variety of diseases, especially recurrent dysentery, with or without abscess, that it did not seem at that time to be particularly diagnostic of abscess. He also speaks of the swelling noticed at the costal border. This swelling appeared in only a few of my cases, and was generally in the single abscess type, which almost invariably was followed by recovery. In this type of case there were no chills, but in the multiple abscess type with dysentery chills and irregular fever were always present. In two of the cases where there was dysentery, the colon was entered and irrigated. In one of these cases the great benefit derived from the irrigation was shown on autopsy, and in the other a cure was effected by this procedure.

"In my opinion this is the best method of treating those obstinate cases of recurrent dysentery which so often baffle medical skill. The most practical way to accomplish the end is to perform right inguinal colotomy. It is my belief that a large number of lives may have been saved in the Philippines during the late war had the surgical treatment been adopted. As it was, the antagonism of the great majority of our medical men to the introduction of surgical methods in the treatment of a disease which had hitherto been considered as belonging especially to the province of the physician, was too strong to be overcome. It is to be hoped that by this time a different spirit prevails among them, and that when necessary the surgeon is promptly called upon to aid in the treatment of the dread tropical disease which we are considering. When the attacks of dysentery have been stopped and the ulceration of the bowel healed, then the danger from that extremely fatal complication, abscess of the liver will have been greatly lessened."

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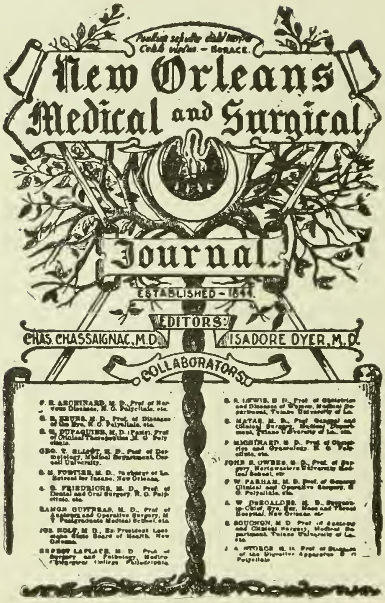

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The American Society of Tropical Medicine.

1909.

HENRY B. WARD,
STATE UNIVERSITY,

The American Society of Tropical Medicine.

Papers Read Before the Society and Published Under Its Auspices.

Volume 4, 1909.

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A BRIEF REVIEW OF A YEAR'S PROGRESS IN TROPICAL MEDICINE.

By JAMES M. ANDERS, M. D., LL. D., Philadelphia.

At the outset, I desire to express my deep indebtedness to the Council and members of this Society for the honor conferred in reëlecting me President, and for helpful suggestions and invaluable assistance in carrying on the duties of that office. An examination of the proceedings of this body since its inception cannot fail of convincing the most skeptical that substantial progress has been made in Tropical Medicine during recent years in our own country. The American Society of Tropical Medicine has, by its work and discussions, created a lively interest in this special branch of medicine, and has served to stimulate investigations that will result in actual scientific achievements. There can be no longer entertained a well-founded fear that the Society will not speedily justify its existence.

The urgency of the matter of acquiring sufficient knowledge to supply the United States Government with more well-authenticated facts and authoritative advice is not sufficiently appreciated. Obviously, workers would multiply and knowledge increase as the result of the establishment of schools of Tropical Medicine in America. A similar effect would be produced by the founding of a successful Journal of Tropical Medicine. I would respectfully suggest the appointment of a representative committee from this Society to consider these two suggestions from the standpoints of feasibility and practical utility. It is worthy of record that quite recently there has been founded the Société de Pathologie Exotique in Paris, with Dr. Laveran as President. The first bulletin, containing the proceedings of the meeting of this Society held January 22, was issued in March, 1908.

Tropical Medicine in America, which owes its interesting development to the closer relations each succeeding year, commercially, socially and professionally, of the United States with the peoples of Cuba, Porto Rico, the Philippines and Panama, has continued to attract increasing attention on the part of scientific investigators during the past year. The progress has been influenced mostly by the brilliant researches of men connected with the various departments of our governmental service resident in tropical climes, many of whom are either active or honorary members of this society. In an address to the British Medical Association Sir Patrick Manson stated that the United

States—the youngest of the colonizing powers—was the first to grapple with the ankylostoma problem, and, "by her efforts in Cuba, Porto Rico, Havana and Panama, had set them an example and shown what can be done by intelligent and energetic tropical sanitation." In this connection, reference may be appropriately made to a quite recent article on the subject of "Sanitation of the Tropics, with Special Reference to Malaria and Yellow Fever," by Dr. William C. Gorgas[1], in which he describes a model organization, and further states that while yellow fever has been successfully stamped out of Panama and Cuba, it could have been done more expeditiously with a better organization. Gorgas also contends that in the municipalities "the same measures that are directed against yellow fever will avail against malaria."

A review of the sum total of the results obtained by individual investigators would necessitate an unwarranted infringement upon the brief time allotted for the scientific papers and discussions of this meeting. In this brief resumé of the definite and noteworthy advances, I cannot hope to do more than enumerate such as have impressed me as being of the greatest practical significance. I shall not venture to indicate their precise scientific or biological importance, but rather make brief reference to their clinical value and bearings.

Following the pointing of the way to future developments in the line of the study of the parasitic protozoa *in vitrio,* Dr. E. L. Walker has described an ingenious method of cultivating amebæ on cover glasses. Without stopping to give the details (which are published in the *Journal of Medical Research,* February, 1908) of his method, suffice it to state that his results throw doubt on the accuracy of the observations of Schaudinn, who classified the parasitic amebæ of man into a non-pathogenic form—*Entamœba coli,* and a pathogenic form—*Entamœba histolytica.* Walker concluded, from a study of forty-four cultures of parasitic amebæ, that there are no less than ten distinct species. The pathogenic varieties, he thinks, can be finally determined only by the correlation of cultural, morphological, experimental and anatomical studies.

In January, 1908, Ashburn and Craig[2] reported the results of personal observations upon some twenty-two cases of "spotted fever," of Montana, and seven cases of tsutsugamushi disease. After giving a brief account of each, they point out the wide geographic separation of the two affections, and then proceed to summarize the points of differentiation by means of elaborate parallel tables. While conceding that they present many points of resemblance, "these are not sufficient to overbalance those of difference." Against either of these two diseases there is a single, common means of prophylaxis, to-wit: Avoidance of the infected region. Ashburn and Craig assert that this is much easier in the case of tsutsugamushi disease than in that of spotted fever, "because the dangerous regions are so much smaller and plainly marked off by the very flooding that makes them dangerous, and, moreover, they are not residence sites." In concluding their interesting contribution, these investigators suggest that medical men in the Philippines, where certain cases bearing a resemblance to tsutsugamushi are seen, keep the matter in mind, should opportunities for investigating them be presented.

J. M. Phalen and Henry J. Nichols[3] discuss at length the pathologic findings in cases of schistosomum japonicum, including the report of a case under their personal observation, and draw a contrast between these and those of infection with closely allied schistosomum hematobium. In their case the liver was the organ to bear the brunt of the infection, it being found to be cirrhotic, thus confirming the observations of other observers. Katsurada believes that the cirrhosis of this disease is caused by the ova acting as emboli, although he mentions also a toxin which is elaborated by the worm and plays a part in producing the liver changes.

Phalen and Nichols, however, in discussing the pathogenesis of the cirrhosis, think it difficult to account for the destruction of whole lobules in the presence of but a very few ova. The histologic changes presented by the liver in this form of schistosomiasis are in striking contrast with those observed in schistosomum hematobium, according to the observations of Madden, Scheube, Manson and other writers on the subject. On the other hand, in bilharziosis the ova cause profound changes in the intestines and bladder. To account for these differences of the distribution of the ova in the tissues of the body we have the differences in their morphology rather than the location of the adult parasite, since both are found in the portal system, e. g., the branches of the portal vein within the liver and the splenic veins.

Geiger[4] has made "A Preliminary Report on Gangosa and Allied Diseases in Guam." He divides the cases into three groups: 1. Ulcerations which yield readily to antiseptic treatment. This group is caused by the ordinary pus organisms, the *Bacillus pyocyaneus* being the most common.

Group 2. Ulcerations which yield slowly to antiseptic treatment. It is to this category of cases that the term gangosa should be limited, and it is the one to which belong a large percentage of the cases. Geiger announces the discovery of a specific organism which he has named *Bacillus gangosæ.* This organism was found present in all the active cases, and has never been found in any other condition, although Geiger admits that it is doubtful if it can be distinguished from the bacillus diphtheriæ by cultural means.

Group 3. Ulcerations which are only modified by antiseptic treatment. This group is characterized by the appearance of distinct tubercles or nodules, and Geiger thinks that a consideration from all aspects leaves no room for doubting that it is rhinoscleroma.

The importance of the X-rays as a therapeutic agent in chronic infectious granulomata and allied diseases, e. g., lupus, has been generally recognized within the past few years. E. A. C. Matthews[5] reports highly favorable results from this method of treatment and high frequency discharges in the treatment of leprosy. No other measures were used during the time that the patients were under his observation, except that the ulcerating cases were dressd daily with boracic ointment. Matthews claims that this is "the only method yet tried which has produced any real effect on the progress of every form of the disease." It may be remarked that whilst this agent in his cases—seven in all—gave most encouraging results, the majority were not actually cured, but only markedly improved.

The subject of plague has continued to occupy much of the attention of scientific investigators during the past year, but on the whole no notable advances can be recorded. The rat-flea theory of plague, which had acquired the enviable position of a text-book dictum, has been questioned by W. A. Hossack[6], who has endeavored to point out what he regards as fallacies in the evidence in its favor.

He states that the *M. rattus,* which was attacked as the principal disseminator, is in reality almost negligible. On the other hand, as shown by the exact figures furnished by the second report of the Plague Commission's work in Bombay, 70 per cent. of all rats examined and 84.6 per cent. of all rats found infected were *M. decumanus*—the brown rat. Further, that the Commission, in their third report, brought forward a modified *M. rattus* theory to the effect that while a few cases of plague may be caused directly by *M. decumanus,* it is only when the disease has spread from the latter to the house-haunting *M. rattus* that man becomes seriously infected.

Hossack then disproves the so-called modified M. rattus theory to his own satisfaction, at least. His observations on the rat-flea tend to upset the flea theory and to indicate that there is not one, but many, modes of plague-infection.

In a short abstract of the Plague Commission's work in Bombay, G. F. Petrie, a member, replied to the criticisms of Hossack of the rat-flea plague. He did not regard seriously the skeptical attitude of Dr. Hossack after weighing carefully the experimental evidence of the Commission. One fact relating to the mode of infection of more than passing practical importance, he emphasized, namely, that while the essential agent in the transmission of plague to man is the rat-flea, the Commission do not wish to deny the possibility of other methods of transmission of infection being operative, "but they maintain that these methods are so rarely effective as to be quantitatively negligible from an epidemiological standpoint." (Petrie.)

S. Browning-Smith[7] discusses rat-destruction operations in the Punjab, and states very decidedly that they are by far the easiest measures to carry out and the ones most readily accepted by the people. His article deals with three methods of carrying out rat-destruction, namely, chemical poisons, traps, and bacterial substances, producing epizootic disease among rats. With reference to rat-poisoning campaigns, it should be pointed out that, while the locality treated is rendered fairly rat-free, the expedient is only a temporary one. Hence, its operations have been limited to two periods during the season—one in September-October and another in February—thus anticipating the two periods of greatest rat fecundity and plague incidence—autumn and spring. The removal of rats by trapping, to be effective, must be carried out continuously, and Browning-Smith recommends that trapping should follow a poisoning campaign, so as to keep the rat population at a minimum. Trapping, it is suggested, should also form an important part of urban sanitary procedure in all towns and villages that are or likely to be centres for diffusing plague-infection. No infective disease, non-communicable to man and animals, has as yet been introduced among rats, although the establishment of a fatal epidemic in this way is much to be desired.

Browning-Smith presents statistics which indicate conclusively that more or less immunity results from systematic rat-destruction. There are certain other measures quite as effective, e. g., evacuation and inoculation, but they involve more interference with the comfort of the people, hence less acceptable than the methods of rat-destruction.

Since the plague bacillus can maintain a successful existence in the living bodies of fleas and rats, the destruction of the latter creatures will tend to exterminate the disease. In this connection, Hossack's recent observations in Calcutta upon disinfection with 1 in 500 acid perchloride of mercury solution in oriental conditions are of particular interest.

The diminished virulence of plague during the last spring months in India is noted by several writers, and this has been attributed to various influences. Nesfield[8] invites attention to the natural habits and instinctive tendencies of the rat to account for the mitigating tendency of the plague epidemic during the last spring and early summer months. He points out that the decreased virulence of plague during the spring season proceeds hand in hand with the falling off in food supplies, and that the outbreak in the winter is "due to the storing of a great part of the autumn harvest in the dwelling-houses, coupled with the scarcity of food for rats in the field. The natural consequence resulting is a great exodus of the rats from the fields into the villages." It is probable that during the drying process, which lasts from two to six weeks, the rats are strongly attracted, having free access to the grain. Nesfield thinks that famine killed off many rats last spring, and this fact, coupled with a scarcity of food, may account for the mildness of the epidemic at that season of the year. The lessons to be gathered by the natives from these observations are not to store grain in their dwelling-houses and to make windows in their homes rat-proof. Nesfield believes that the observance of these, and only these, two things will stamp plague out of India.

The success attending wholesale rat-destruction in San Francisco during the epidemic of plague just ended, under the supervisory control of Dr. Blue, is undoubted. For example, when systematic efforts at rat-destruction were instituted about ten thousand rats were captured each week, whereas at present only about two thousand are brought in weekly. The last case of plague reported from San Francisco, be it remembered, began on January 30, 1908.

The opinion of Haffkine, that we shall never get rid of plague unless universal inoculation be adopted, is being called into question. While its efficacy as a temporary expedient cannot be doubted, e. g., where a man is forced to enter a plague-infected district, when practicable, as Buchanan has pointed out, evacuation is to be preferred where this dread disease is prevailing. Perhaps the best position to take with reference to the question of the prevention of plague is that no single anti-plague measure should be adopted to the exclusion of all others. In this connection it is interesting to note that the records of plague inoculation in the Punjab indicate clearly that the people are gaining confidence in its efficacy as a protective measure. For example, "in 1906 the total number of inoculations was 22,951; in 1907, 40,032, while in the present year, although the incidence of the disease has been much less alarming, it has already risen to 45,775.",

In an interesting address before the "Section of Tropical Diseases" of the British Medical Association, Daniels[9] stated that in practically all tropical diseases some implication of the lymphatic system did or might occur, whether they were due to bacteria, protozoon or metazoan parasites. Both lymphangitis and adientis, due to skin breaches of continuity from biting arthropods (e. g., ticks, flies, mosquitos) were more frequent than in England. The lymphatic diseases, more especially associated with tropical conditions, were those due to metazoan parasites. Daniels contended that lymphatic obstruction was not confined to the tropics; he himself had seen two cases in England. The real problem, therefore, was why lymphatic obstruction sufficient to cause chronic edema, a rare disease in England, in the tropics might affect 5, 10 or 15 per cent. of the population. He thought the explanation was to be found in the relationship existing between elephantiasis and filariasis—a disease unknown in England. This view was supported by facts of geographical, topographical, racial and sex distribution as well as by those pertaining to the known intermediate hosts.

The theory of the relationship of elephantiasis and filariasis, however, was opposed, notably by Prout, of Liverpool, who believes that elephantiasis is a streptococcal disease.

Phalen and Nichols, of the present United States Army Board for the Study of Tropical Diseases as they occur in the Philippine Islands, in an article on "Filariasis and Elephantiasis in Southern Luzon," state that the results of certain investigations made by them support the generally accepted view that elephantoid disease is directly due to filarial infection. They found that the subject of elephantiasis showed a lesser percentage of filarial infection than the general population. Whilst filariasis has a pathologic and clinical interest principally from the possibilities of its sequelæ, it is to be recollected that it is not as rare a disease in the Philippine Islands as has been supposed. Phalen and Nichols believe that the Bicol provinces and Davao are the largest and most important endemic foci of filarial disease in these islands. Finally, they believe that the filaria nocturna is the common filaria of the islands.

Castellani[10] reports interesting observations on palliative treatment of elephantiasis. Hypodermatic injections of various antiseptics, with the idea of destroying the organisms, failed to bring about the slightest improvement in any case. Based on the anatomical features of elephantiasis, more particularly the enormous increase of the fibrous tissue, it occurred to Castellani that thiosinamin, which, according to Hebra, Van Horn and others, has the power of softening various kinds of fibrous tissue, thus facilitating its absorption, might be useful in the treatment of the disease, especially in cases of long standing. Thiosinamin injections were found to be very painful, and hence fibrolysin, which is a water-soluble combination of thiosinamin with sodium salicylate, was substituted. Fibrolysin is obtainable in sterile glass ampullæ, each containing two cubic centimeters of liquid, corresponding to 0.2 gram of thiosinamin. With an ordinary antitoxin syringe, Castellani makes the injections in various parts of the affected regions, after which a sterile pad of gauze is applied at the place of injection and the whole limb is tightly bandaged with flannel. These injections are made every day or every other day, according to the features of the case, for about a month, and then discontinued for a week, "during which time the use of flannel and india rubber bandages was continued." Subsequently, portions of the redundant skin were removed surgically. In five out of seven cases the thiosinamin injections induced a fairly well-marked, though transient leukocytosis. Castellani claims as yet only palliative results from this method of treatment, and states decidedly that, without a constant, well-distributed pressure after methodical injection, best obtained by the application of hard pads and by careful bandaging, no marked improvement is to be expected.

The organism discovered by Castellani[11] in 1905 in smears from yaws papules (closely resembling Treponema pallidum) has, after confirmation by Wellman[12] and Ashburn and Craig[13], been accepted as the specific cause of this disease. It bears the name of Treponema pertenue. Pierrez had previously drawn the clinical distinction between yaws and any of the recognized forms of syphilis.

In his second edition of "Tropical Diseases," Sir Patrick Manson gives thirty-two members of the family Anophelinæ, which have "been shown, with more or less precision, to be efficient hosts of the malaria parasites." Mr. Charles S. Banks[14], entomologist in the Biological Laboratory of the Bureau of Science of Manila, has shown conclusively that *Myzomyia ludlowi* should be added to the list. Among other interesting facts observed were "the development of the gametocytes into the ookinete and into the sporozoites has been definitely traced in this mosquito, and one person has been experimentally infected by the bite of an infected insect."

The subject of hemoglobinuric fever is one that has a peculiar interest for American internists and the general practitioners of warm countries everywhere. Plehn has recently discussed its causes, prevention and treatment *in extenso,* and his main conclusions are worthy of notice. After showing the malarial nature of blackwater fever, Plehn affirms distinctly that, with few exceptions, the tendency of the European to sicken with blackwater depends on the length of his sojourn in the fever district, the condition being more prevalent when the colonists are of longer settlement than when there is a fresh arrival of newcomers. There are two weighty objections against the malarial origin of blackwater, namely, the frequent absence of malarial parasites from the blood and the failure of quinin therapy; but Plehn has shown by elaborate statistics that the plasmodia are always found when the blood is taken before the commencement of the hemolysis, while they are regularly absent during the height of the illness. The parasites may be seen to disappear spontaneously on the second or third days of the illness without medication.

It is owing to the dissolution of the blood that quick spontaneous disappearance of the malarial parasites from the circulation occurs, and this fact answers the principal objections to the theory that malaria is the origin of hemoglobinuric fever. From the facts adduced by Plehn, it would appear that blackwater fever develops only after a certain time, "through the action of latent malaria without preceding fever." Protection against this disease can be established by shortening the period of residence in the country where it prevails, e. g., Central Africa.

A certain degree of immunity can also be procured by leave of absence for variable periods of time, and by guarding against violent climatic changes. Plehn, however, bases chief reliance upon systematic quinin prophylaxis to obviate the dangers of malaria and blackwater in particular.

Yersin and Vassal[15] were given an excellent opportunity to study five cases of a disease which they diagnosticated as typhus fever. These occurred among the thousand coolies who had been imported into Nhatrang, Annam, from Tonquin. They tried repeatedly to reproduce the disease in laboratory animals, such as the rat, the guinea pig and the rabbit, but without the slightest success. Experiments on human beings, however, gave contrary and positive results. For example, they injected half a cubic centimetre of blood from one of the patients under observation into a healthy person of the same nationality, the donor being in the second day of the disease. An attack of fever precisely similar to that from which the donor was suffering occurred in the recipient at the end of two weeks. The febrile movement lasted for eleven days, and then ended by crisis, just as in the naturally acquired infection. A second similar experiment gave an incubation period of twenty-one days. The febrile paroxysm did not differ from that of the primary experiment, and ended by crisis on the twelfth day. The specific cause of the disease was not discovered. Yersin and Vassal suggest that the disease is probably transmitted by insects—an hypothesis which would explain the extreme contagiousness of the disease, and also its disappearance with improved sanitation in jails, asylums, barracks and like institutions.

The third report of the permanent commission for the suppression of uncinariasis in Puerto Rico[16] contains much interesting matter. The commission advances the theory that the anemia of uncinariasis is due to hemolysis, and not to hemorrhage, as was formerly believed. It cannot, however, be denied that a capillary hemorrhage from the intestines continued for long periods of time may and does produce severe anemia.

In his paper presented to the British Medical Association on "Sanitation in Reference to Ankylostomiasis in the Tropics," which paper I have already cited, Sir Patrick Manson[17] stated that the most important measure was the proper disposal of infected excreta. So long as these are scattered over the soil it would appear useless, in his opinion, to employ any other methods having for their object the stamping out of this disease. Manson pointed out the significant fact that the eggs, in the absence of oxygen, would not hatch, or, if hatched out, the larvæ would have no opportunity to get at the human skin. He thought it altogether feasible to get the coolie or native to drop his excrement into a hole in the ground with no pollution of adjacent soil. He added: "That method costs nothing, and, if uniformly and properly and permanently carried out, would be absolutely effective."

W. F. Law[18], who read a paper on "Ankylostomiasis in British Guiana" at the same meeting, expressed the opinion that the question of prevention might be summed up in one word—latrines.

Tropical dermatomycoses have recently been considered by A. Castellani[19], who introduces his remarks with the statement that our knowledge of the subject is far from complete, due partly to lack of opportunity to observe such diseases in temperate climates, and partly to the fact that as soon as patients move from a tropical into a cold climate the clinical features of such eruptions change greatly. According to the results of his investigations into the tropical diseases caused by fungi of the genus Trichophyton, there are six sub-classes, as follows: (1) *Tinea cruris,* or "dhobie itch"; (2)*T. albigena;* (3) T. of Sabouraud; *(4) T. imbricata;* (5) *T. intersecta;* and (6) *T. nigro-circinata.* His observations indicate clearly that tinea cruris or dhobie itch is to be separated from the ordinary forms of tinea corporis. Mixed infections of tinea cruris and tinea circinata have been observed. Castellani describes two species of tinea cruris, and details at length the communicability, diagnosis, complications and treatment of the disease.

Tinea imbricata, first accurately described by Manson, has lately manifested a much extended distribution, and it will be of interest to this audience to note that cases have been reported from Brazil and other parts of tropical America. Tinea intersecta, first described by Castellani in 1907, has since been made the subject of further study and observation by him, having come across cases among the natives of Ceylon. His clear description of the clinical features and method for the detection of the fungus (which cannot be quoted here for want of space) will render the recognition of the condition free from difficulty. Finally, Castellani, in his paper, described a new form of tinea, for which he suggests the term tinea nigro-circinata.

J. H. H. Harrison[20] reports a case of myiasis in a negro woman who had suffered from a small chronic ulcer on the right cheek. On admission the patient presented a huge, foul cavity, four inches in diameter, exposing the bones of the cheek and face. On syringing the excavation with chloroform water, 100 larvæ of the screw-worm were removed, and upwards of 300 worms in all were recovered. The patient gradually sank and died.

Attention may be invited here to an agreement entered into for three years between Great Britain and Germany for the purpose of combating sleeping sickness in their African colonies, operations to be commenced November 1, 1908. The measures adopted were: "(1) Establishment of segregation camps, especially on the boundaries of the British and German territories. (2) Prevention of infected natives passing into uninfected districts. (3) Notification of infected areas. (4) Effective measures for dealing with animals serving as carriers or alternative hosts of the trypanosome; interchange of experiences, literature and knowledge gained by reasearch work."

A paper of great interest in connection with the subject of Gland Palpation in the Diagnosis of Human Trypanosomiasis, by John L. Todd[21], has recently been published. As is well known, the Liverpool School of Tropical Medicine maintains three important principles, as follows: "(1) That gland palpation is the most efficient means of diagnosis of human trypanosomiasis. (2) That gland palpation is a most important method of rough diagnosis, since, in the Congo Free State at least, every native with distinctly enlarged glands, other causes being absent, must be considered to be a case of human trypanosomiasis until the contrary is proved. (3) That quarantine measures, dependent in a large measure for their efficiency upon gland palpation, should be immediately applied."

After a careful review of current views in support of these principles, as well as those that strike a discordant note, Todd reports certain new facts which tend to confirm them. It is obvious that, with the opening up of Africa, for example, and the increased movements of natives over long distances, sleeping sickness will continue to spread, and the writer urges Europeans to do all that is possible "to prevent this extension of the disease which largely results from their presence." It is generally conceded that, of the many measures employed to arrest the spread of this disease, by far the most important and effective is quarantine; and Todd argues that its efficiency will be dependent upon the application of gland palpation, since it is believed that the number of cases which will escape diagnosis is exceedingly small.

As bearing upon the probable remaining duration of life in 102 untreated cases of sleeping sickness, it was found, roughly, that patients commenced to die in a year; "two-thirds of them die within three years, while one-third of our patients are alive and well from thirty to forty months after they were first observed." In the mildest form, the symptoms are negative, save slight irregular or intermittent fever and enlarged glands.

The well-known increase in the large mononuclear leucocytes, which is found in cases of infection with the protozoan parasites, has not been observed by Yakimoff[22] in experimental trypanosome infection of certain animals. He employed Trypanosoma brucei and Trypanosoma equinum, inoculating them into nine white mice, four white, mottled and gray rats, ten guinea pigs, five dogs and two foxes. These systematic studies showed a variable degree of oligocythæmia and oligochromæmia, and leucocytosis, which reached its maximum on the third day, to be followed by a diminution in the number of these cells (persisting until the death of the animal). No increase in the large uninuclears was observed, but in the absolute and relative numbers of the polymorphonuclear cells. The latter showed, first, a primary increase; second, a diminution; and, third, a secondary increase. The lymphocytes were decreased in number.

The experimental treatment of trypanosomiasis in rats by a committee of the Royal Society has led to encouraging practical results. After employing a number of substances with varying results, the sodium antimonyl tartrate in one per cent. solution was tried. They found that this preparation surpassed all others in its effects upon the trypanosomes in the living body. Thirty-nine rats injected with *Trypanosoma evansi* and *Trypanosoma brucei* were treated with this substance. While some died of other diseases than trypanosomiasis, a satisfactory percentage were living at periods varying from twenty-one to fifty-two days after the commencement of the disease.

Professional interest in the subject of the etiology of beriberi continues unabated. Fraser and Stanton[23] have obtained interesting results from their studies of beriberi occurring in immigrant laborers on the Malay peninsula, it being possible for them to obtain exact information as to their dietary and their methods of preparing the same. The disease prevailed only among those who ate white rice, while no case occurred among 273 persons on parboiled rice under similar conditions. Again, in coolies who ate white rice for less than eighty-seven days the disease failed to develop. Systematic examinations of the blood and urine of beriberi cases did not show any organisms other than those recognized as the causative agents of other diseases. No cases developed as the result of contact, hence the authors believe that beriberi is non-communicable. Their investigations also showed that place *per se* had no influence upon the development of the disease. The writers, therefore, conclude that beriberi, as it occurs in the Malay peninsula, has, if not its origin in, at least a close relationship with, the consumption of the white rice, and suggest that further studies along these lines should be undertaken. Holst and Frolich[24] have published some interesting feeding experiments on pigeons and chickens, in which a disease was produced which resembled tropical beriberi, and, according to their results, the advocates of the etiologic relation of mouldy rice and beriberi seem to have the advantage over those who believe in the bacterial nature of the disease.

Dr. Edward J. Wood[25] presented an interesting communication on "The Appearance of Pellagra in the United States" to the College of Physicians, of Philadelphia, November 4, 1908, in which he also referred to its prevalence in Italy and Roumania. Of 196 cases collected by him from the literature and personal letters, seventy occurred in North Carolina. While this disease is met with in two varieties in the Southern States, the acute fulminating or "typhoid" is the more common; it runs a course from a few weeks to three months, and the primary attack invariably proves fatal from exhaustion. Clinically, this variety is characterized by symmetrical erythema, stomatitis, and often salivation, diarrhea and severe toxic features. This form is unlike anything described in Italian literature, hence virtually a new disease. The chronic variety is similar to that described by the Italians. The subject of pellagra is one of unusual interest and one that has attracted widespread attention during the past year, but, inasmuch as it will be made the subject of a symposium on this occasion, I shall not consider it further here.

1. *Journal of the American Medical Association,* April 3, 1909.
2. *The Philippine Journal of Science,* January, 1908.
3. *Ibid,* July, 1908.
4. United States Naval *Medical Bulletin,* January, 1908.
5. *Indian Medical Gazette,* August, 1908.
6. Transactions of the Society of Tropical Medicine and Hygiene, Vol. II, No. 11, January, 1909.
7. Report to the Government of the Punjab, *Indian Medical Gazette,* August, 1908.
8. *The Journal of Tropical Medicine and Hygiene,* September 15, 1908.
9. *Journal of Tropical Medicine and Hygiene,* September 15, 1908.
10. "Observations on Palliative Treatment of Elephantiasis," *The Philippine Journal of Science,* September, 1908.
11. Editorial, *New York Medical Journal,* March 28, 1908.

12. *Journal of Tropical Medicine*. Vol. VIII., p. 345.
13. *Philippine Journal of Science,* October, 1907.
14. Editorial, *New York Medical Journal,* April 11, 1908.
15. *Philippine Journal of Science,* April, 1908.
16. Editorial, *New York Medical Journal,* March 7, 1908.
17. *The Journal of Tropical Medicine and Hygiene,* September, 1908, page 271.
18. *Loc. cit.*
19. *The Journal of Tropical Medicine and Hygiene,* September, 1908, page 261.
20. *The Journal of Tropical Medicine and Hygiene,* October 15, 1908.
21. *The Journal of Tropical Medicine and Hygiene,* August 1, 1908.
22. *Archives des sciences biologiques,* XIII, 3.
23. *Lancet,* February 13, 1909.
24. Editorial, *New York Medical Journal,* January 18, 1908.
25. *New York Medical Journal,* March 6, 1909.

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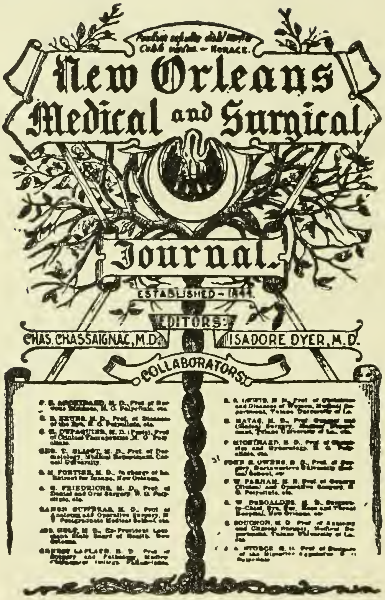

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AGRICULTURAL ASPECTS OF THE PELLAGRA PROBLEM IN THE UNITED STATES.*

By Carl L. Alsberg, M. D.,
Washington, D. C.,

Expert, Drug and Poisonous Plant Investigations, Bureau of Plant Industry, U. S. Department of Agriculture.

(*Published under the Imprimatur of the American Society of Tropical Medicine.*)

As I wish to speak on pellagra from the aspect of the agriculturist, I am going to make the assumption, right or wrong, that pellagra is caused, directly or indirectly, by the consumption of Indian Corn. I wish, however, to make myself perfectly clear upon this point. I am not asserting that corn is the only or even the most important ætiological factor. My own personal experience with the subject has, as yet, been inadequate for me to have an opinion of my own. I am making the assumption merely as a working hypothesis. I am going to assume further that good corn is wholesome, but that spoiled corn is an important factor in the development of pellagra. I am perfectly well aware that the zeist theory of the ætiology of pellagra is not universally accepted, and I am furthermore perfectly well aware that the supporters of this theory are divided into two unequal groups, a small one asserting that a corn diet is in itself an important factor; and a far larger one which makes spoiled corn alone responsible. However, I think it is no

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overstatement of the facts to say that the great majority of the students of pellagra incline to the belief that spoiled corn when consumed by poorly nourished and badly housed individuals is the most important ætiological factor. This being so, it is not for me to pass judgment on the merits of their attitude. I can but accept it provisionally, disclaiming, for the present, any responsibility for it.

Now, making this position, be it right or wrong, our starting point, let us ask ourselves the question why it is that, though maize has been grown and consumed in this country for ages, pellagra has not appeared until within the last few years. I realize perfectly that, logically, I ought to prove that pellagra is actually a new disease and has not merely been overlooked until the last few years. This, however, is again a clinical proposition that lies outside the scope of my work. I can but assume that the clinicians of the past were good observers and that therefore pellagra is a newcomer. Why then is it a newcomer? Have there been in recent years changes in our methods of dealing with corn which, on the zeist theory, would explain the appearance of pellagra?

Are we to-day planting new varieties of corn more subject to spoiling than the old ones? Have new methods of corn culture come into vogue? Are climatic conditions different? Has corn culture spread to new territory unsuited to it? Is the method or time of harvesting other than it used to be? Are the methods of storage and transportation changed? Does the consumer cook or prepare corn food in new ways?

These are some of the possibilities that must be taken into account. Let us consider them seriatim and see how far they support, individually or collectively, the zeist theory and how far, assuming the correctness of this theory, any changes that we may find account for our recent outbreaks of pellagra.

Let us first consider corn culture in the south where pellagra has appeared and where corn forms twenty-three per cent. of the diet of the Tennessee and Georgia mountaineer and 33.5 per cent. of the negro's.[1] Conditions in some of the southern States resemble those in New England and the northern Atlantic States in that an amount of corn insufficient for local consumption is produced. This statement is difficult to prove in the absence of statistics upon the movement of crops within the country. The statistics on the shipping of corn out of the county where grown show us that in both these sections of the country but a very small portion of the crop leaves the home county.[2] The inference is that much corn is imported from the corn belt; and this is the opinion of crop and milling experts. Nearly all the corn grown in the south must therefore be consumed and milled where grown. Under such conditions changes in agricultural methods are less likely to be made than when the produce is exported into the markets of the world. Corn, furthermore, has been until very recently, possibly, a minor crop in the south. It was more profitable to exchange cotton for corn than to grow corn, another state of affairs not likely to stimulate changes in agricultural methods.[3] Moreover, the further south we go the poorer the average yield per acre. Statistics do not show any marked increase in the yield of the last ten years such as one would expect were corn culture changing or improving rapidly in the south.[4] And nevertheless despite these factors which make for conservatism in agriculture, the educational influence of the southern experiment stations has been effective in bringing about some change though not as much as in the corn belt proper where these conservative factors are not effective.[5] The varieties of corn planted, which, as we shall see, have changed so much in the corn belt, have not left the south uninfluenced. The methods of corn culture have in a measure changed, due to improved methods of agriculture involving the rotation of crops. A man farming on this principle wants to get one crop off the land so as to be able to get the next one in as soon as possible. The result is a tendency, in a few sections to-day, to harvest the corn before it is thoroughly ripe, whereas formerly it was allowed to dry out on the stalk till late in the fall. A similar effect in causing a too early harvesting of corn is brought about in a few sections by the cessation of the old practice of topping. Topping consists in cutting off for fodder that portion of the stalk projecting above the ears. The ears were allowed to ripen and dry on the remainder of the stalk. They were then husked in the field, and the stover used as forage. Experiment stations have demonstrated that this form of procuring fodder is unprofitable; and it will in time die out.[6] More and more corn is being shocked instead of being allowed to ripen on the standing stalk. The result is again a tendency to harvest more unripe corn than formerly. However, it is but fair to say that despite the efforts of the stations these changes in southern agriculture have been very slight. Of the remaining factors of our list, transportation, inasmuch as most of the corn produced is probably consumed locally, can hardly be of importance. Still it is worth while pointing out that, as we shall see in another connection, transportation in the warm and sometimes also moist southern climate may be a more important factor in spoiling corn than it is in the colder north. Methods of milling in the conservative south have probably also changed less than elsewhere. This applies particularly to the removal of the germ before the grinding of the endosperm. While in the north nearly all the corn for human consumption is treated in this way, in the south the old fashioned form of corn meal is still very popular.[7] The great significance of this fact, I shall have ocasion to recur to later.[8] The south is climatically peculiarly well suited to corn culture and the climatic conditions must be exceptional indeed to prevent proper ripening of corn. How important ripening is, we shall soon see. And finally I have been able to learn of no changes in the preparation of maize food which seemed significant.

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[1] C. S. Woods. Food Value of Corn and Corn Products. *Farmers' Bulletin, No. 298, U. S. Department of Agriculture,* p. 7.

[2] *Yearbook of the Department of Agriculture,* 1907, p. 610. W. O. Atwater and Charles D. Woods. Dietary Studies with Reference to the Food of the Negro in Alabama. *U. S. Department of Agriculture, Office of Experiment Stations, Bul. No. 38,* 1897, p. 17.

[3] S. M. Tracy. Corn Culture in the South. *U. S. Department of Agriculture. Farmers' Bulletin No. 81,* 1898, p. 1.

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[4] *Yearbook of the U. S. Department of Agriculture*, 1901, p. 611.

[5] *Alabama College Station Bulletin*, No. 88. *Mississippi Station Bulletin*, No. 33.

[6] S. M. Tracy. Corn Culture in the South. *Farmers' Bulletin, No. 81, U. S. Department of Agriculture*, 1908.

We have then found changes in the corn grown in the south mainly in the harvesting of greater quantities of imperfectly ripened and cured corn, and possibly also in new varieties grown. Even these changes are, however, not very extensive. Most other factors remain unchanged. Is this true of imported corn, which as we have seen is increasingly imported into the south as well as into New England? Can we find new conditions in corn imported into the south from regions further north, which are capable—always granting the correctness of the zeist theory—of accounting for the outbreak of pellagra?

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[7] Atwater and Woods, *l. c.*, p. 19. H. B. Frissel and L. Bevier. Dietary Studies of Negroes in Eastern Virginia, *U. S. Department of Agriculture, Office of Experiment Stations, Bulletin No. 71*, p. 8, 1899.

[8] H. W. Wiley. Composition of Maize, *U. S. Department of Agriculture, Bulletin No. 50*, p. 10. C. S. Woods, *l. c.*, p. 12.

I think we can. Such changes will be particularly significant if we consider that in the past generation the amount of corn imported into the south has been increasing. In fact there has been considerable change all over the country. Corn was formerly produced sufficiently for local needs and corn meal was made locally. Naturally, under these conditions the best corn was selected for human consumption. In recent decades corn has more than ever before become an article of commerce, a condition of affairs which certainly does not tend to keep up quality. Therefore let us take up again our series of possibilities applying them this time to corn culture in the corn belt.

Varieties of corn planted have been changing considerably in the last decades. Originally in New England the flint corn was and still is grown. One of its characteristics is its excellent keeping quality. In the corn belt this variety is not grown to any considerable extent. Consciously or unconsciously the effort of the agricultural experiment stations has been to increase the oil content of corn. The result is a decided increase in the amount of corn oil which may be obtained from the grain and a corresponding increase in the caloric food value of the grain, a most important economic factor because so much corn is used to fatten domesticated animals. What may be accomplished by systematic selective breeding along these lines is seen in some work done recently by Louie H. Smith, at the Illinois Agricultural Experiment Station[9]. In ten generations the oil or fat content was raised from a minimum of 4.70 per cent. to a maximum of 7.37 per cent., a gain of 2.67 per cent. Now, this change in the oil content of the grain may well be of importance to pellagra. When corn becomes mouldy it is always the embryo that is affected first. It is into the embryo that the fungus first makes its entry and there it flourishes best. Not merely does the fungus flourish best in the embryo but the greater part of the toxic material is in the decayed embryo. That spoiled corn contains toxic substances was easily proved by Neusser, Lombroso, Erba, Babes, and others. Whether these toxic substances are capable of producing typical pellagra is an entirely different question, a question that we begged when we started with the assumption that pellagra is due to spoiled corn. Be this as it may, the toxic material is mainly in the germ. Now as it happens, the greater part of the oil is located in the embryo. Probably, therefore, a variety rich in oil is also one with a large germ. It is, therefore, not unreasonable to assume that such a large embryo variety of corn would, when it does become mouldy, produce a greater amount of this poisonous material. It is of course true that in the process of milling the germ is more or less completely separated and used to make corn oil and cattle feed. However, this is not true of corn milled in the south or for the southern market. The milling of corn differs from that of wheat in that it is not so centralized. Corn meal is milled in many places throughout the country. When the germ is not separated the amount of it to be found in different grades of meal is different. The best grades will have least and the poorer grades most. This matter has been investigated by Dr. Stefano Balp, of Bergamo, who was able to show that the toxicity increased with the diminution in quality going parallel with the embryo content.[10] Of course the poorer parts of the population purchase the cheapest and poorest grades of flour and the most toxic. What the material is, out of which the microorganisms manufacture the toxic principle or what this toxic principle itself is, chemically, we do not know. There have, to be sure, been a long series of researches upon these substances. They have been carried out by Cesare Lombroso, Neusser, Babes, Erba, Antoniu, Mario Serena, Elena Manicatide, and others, but in no case has any single substance been definitely isolated or characterized chemically. There is some evidence that some of these toxic substances are related to the fats, or at least have similar solubilities. This is a possibility worthy of future investigation in the light of the work of Faust and Tallqvist[11], upon the rôle of oleic acid in bothriocephalus anæmia. I mention it here merely to point out that the high oil content of recent varieties of corn may also be important in this connection.

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[9] Louie H. Smith. Ten Generations of Corn Breeding, *University of Illinois Agricultural Experiment Station, Bulletin No. 128,* 1909.

And this brings up the question of the keeping qualities of different varieties of corn. As a general rule varieties like flint corn keep best. In Roumania there is a general belief that only the yellow and the white varieties of corn cause pellagra; while the red does not. Von Babes[12] states that as a matter of fact red corn keeps better—in Roumania at any rate—than the paler colored kinds. This is an important line of investigation upon which we have as yet insufficient data, for the subject is a most difficult and intricate one.

We have then in considering our first possibility found that in the corn belt the varieties of corn are changing and changing in a way that may increase the toxicity when the corn spoils.

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[10] *Venticinque anni di lotto contro la pellagra (1881-1906) biella*, 1908.

[11] *Archiv für experimentelle Pathologie und Pharmakologie,* lvii, p. 367 (1907).

[12] *Die Pellagra,* p. 58, Wien, 1901.

The development of new methods of culture in the corn belt may be dismissed briefly. I was able to learn of no radical changes, at least of none capable of throwing light on the matter under consideration.

When we come to consider climatic conditions we find more important factors. Weather statistics show us that for the last seven or eight years we have had a preponderance of cold wet falls and sometimes late springs. Now, corn to ripen properly needs plenty of time for growth and a long warm fall. It is our beautiful Indian summer that is largely responsible for the excellent quality of our corn crop. We have not had the typical Indian summer of recent years, and consequently a fair amount of corn had to be harvested before it was properly ripe. Now, in Italy it is a fairly generally accepted view that corn harvested before it was properly ripe is almost certain to spoil and to produce pellegra. Is it not then a most significant coincidence that our outbreak of pellagra has followed a series of cold, wet falls?

Now, climatic conditions are but one side of the question whether or not we are growing corn in territory unsuited to it. A given district may be unsuited temporarily because for a time there prevail abnormal climatic conditions; or it may be more or less permanently unsuited because only exceptionally does the summer warmth last long enough. Now, the southern part of our country is probably very rarely subjected to such climatic conditions that corn does not ripen properly. As we travel north this becomes less and less true. To-day the corn belt is steadily spreading northward and westward toward the mountains. Every effort is being made to extend it and to develop varieties of corn which will thrive further and further north. The wheat lands of the northwest are not as productive as they were. Hence it is desirable to have a rotation of crops, and corn is one of the crops the introduction of which is being attempted. It is a question whether to-day with the existing varieties of corn the northern limit of safe corn culture has not been exceeded. The cultivation of corn in unsuitable territory is practised extensively in Italy and only in these parts of Italy does pellagra occur. In southern Italy, where maize ripens well, there is no pellagra. Italian and Roumanian investigators maintain that corn harvested unripe is pretty certain to spoil and when consumed to induce pellagra. Is it not likely that with the extension of our corn belt northward in recent years, together with our recent exceptionally cold and wet falls, we have been harvesting more moist corn than in former decades? If this is so may it not have some bearing on the pellagra situation?

Our next point for consideration, the methods and time of harvesting, is intimately associated with the suitability of the territory to corn culture and the climatic conditions. I have already shown that more corn is probably harvested in this country before it is ripe than was the case in former years, partly because of unusual climatic conditions, partly because of the extension northward of our corn belt. These factors necessitate the harvesting of corn too early and its insufficient curing. The great dangers of this procedure I have already pointed out, though it is of course impossible to say how extensive this has been. Corn is very difficult to keep without moulding. This is due chiefly to its great moisture content which is very much greater than that of other grains. It must be thoroughly dried in order to keep well. The parching of corn practised by the Indians was therefore a most rational procedure. Even ripe corn unless it is thoroughly dried is liable to mould. Corn that ripens late in the year has not time to dry properly before it is stored in the cribs and bins. Moreover, it is still the practice of some farmers to store it insufficiently protected from the weather so that during the winter it becomes thoroughly wet. As long as the weather is cold corn does not spoil. As warm weather comes on such corn is very likely to spoil,[13] for the conditions under which it is shipped make its spoiling almost a certainty.

There has been another factor to encourage imperfect curing, the market conditions in the fall. Of recent years the production of corn has probably not kept pace with the demand. The result has been that unusually high prices have prevailed in the fall. These have naturally stimulated early marketing. It is of course evident that shelled corn will dry less easily than corn on the cob in the bin.

Corn is transported in closed cars without ventilation. The grain of corn is a live thing. It is breathing, consuming oxygen, giving off carbonic acid, and as the result of its respiration heat. The heat thus given off increases the rate of respiration till the corn heats up hot enough to create ideal conditions of temperature and moisture for the growth of fungi. Corn transported thus into the northeast may have its tendency to ferment checked by the colder climate. Corn shipped to the south will on the contrary have the tendency to ferment augmented often by the warm moist climate. Quite in conformity with this fact, is the experience of the United States Department of Agriculture with ship loads of corn exported from the seaports of the two sections to foreign lands. Shipments from North Atlantic ports are not so apt to become spoiled; as we go south more difficulty is experienced; while the greatest difficulty is often encountered with shipments from gulf ports.

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[13] **C. P. Hartley.** Harvesting and Storing Corn. *Farmers' Bulletin, No. 313, U. S. Department of Agriculture,* 1907.

We see, therefore, that in the last few years there have been not a few changes in corn conditions. Whether these changes are sufficient to account for our outbreaks of pellagra it is of course impossible to say positively, though they are, to say the least, suggestive. They make the corn imported into the south mainly responsible for the conditions there, though as we have seen there are changes in corn production in the south itself which may well aggravate the situation. Whether this is entirely fair is, in the absence of statistics of the movement of corn within our country, not possible to decide. Certainly there is an analogous case abroad. The Greek island of Corfu used to produce maize of an excellent quality and pellagra was unknown there. Subsequently corn culture was discontinued because wine culture was found more profitable. Corn was thereupon imported and pellagra appeared.

As I have already pointed out New England, as well as the south imports large quantities of corn; and most certainly much of this is spoiled. Why then is not pellagra rife in New England? Pellagra does not occur there for probably the same reasons that it spares the Italian city dwellers though it decimates the surrounding peasantry. The New England population lives under good hygienic conditions, while corn products are only a small part of its daily diet. The reverse is true of the southern darky. In New England in the milling of corn meal the grain is first degerminated. In the south it is usually not so treated. In New England much of the imported grain is fed to stock. The south is notoriously poor in the numbers of its domesticated animals. In New England the climate for a great part of the year does not favor fermentative processes; in the south it does. All these are reasonable explanations.

Having considered the conditions which lead to the deterioration of corn, what remedy is it possible to suggest? The most potent factor in the spoiling of corn is water. An excessive moisture content is very apt sooner or later to lead to mould formation. Of course it is to the interest of the farmer to sell corn with as great a moisture content as possible, for such corn is heavy and will average more bushels to the acre than after proper drying and curing. When it is loaded into cars it straightway heats up, ferments, and spoils, often before it reaches its destination. The dealer who receives such corn naturally often succumbs to the temptation of mixing it with enough good corn so that meal made from the mixture will not be offensive to the taste or smell. The amount of spoiled corn used in this way is very great. The only rational means to combat this evil is to induce purchasers of corn to pay for it according to its moisture content. No progressive large consumer of coal any longer purchases it on the basis of its weight alone. The price paid for coal is to-day regulated by its caloric value. Corn probably varies far more in its caloric value than coal; for its moisture content may vary from less than ten per cent. to more than thirty per cent. Why buy corn in a less rational way than coal? If the price of corn is fixed by the moisture content, this will offer a powerful inducement to the farmer and shipper to dry his corn thoroughly before transporting it because it will greatly reduce his freight charges. It would, probably, very largely put a stop to the spoiling of corn and, on the zeist theory, to pellagra. But it would also be a matter of tremendous economic importance to our country. Of course any preventable disease, pellagra, or any other, is an economic waste; and of course, spoiled corn even when fraudulently sold, represents an economic waste. But the greatest economic waste of all, lies in the unnecessary transportation of water in the form of the moisture in corn. Annually many million gallons of water are hauled from the corn belt to the seaboard, an enormous economic waste, and one that it is to the interest of the public health as well as the public wealth to prevent. The dealing in moist corn has been so great that the exporters have overreached themselves. Not only have they brought it about that American corn fetches a low price in the world's markets, but they have practically closed these markets to this, one of our most important crops.

The remedy is then to cause the corn to be thoroughly dried before transportation. To bring this about, corn must be sold upon a basis of its moisture content. But to make this possible there must be an efficient impartial system of grain standardization. Such a system under the complex conditions of our present civilization can, without doubt, be best carried out by the Federal government. Federal grain standardization would not merely tend to restore to us our lost markets, it would not merely increase our economic efficiency, it would not merely make for higher business morals and greater commercial honesty, but it would also be a most important public health measure. Such legislation would be as truly a potent influence in our public health as a Federal quarantine.

If I have taxed your patience with a discussion of certain features of the corn industry it is because I know that as physicians we are intensely concerned with all that has to do with the public health. Nothing is more important to the public health than the food supply of our people. No element of the food supply is more important than the cereals. In our country corn is one of the most important among them[14]. I trust therefore that anything that affects the quality of our corn is of some interest to American physicians. So I do not feel that I need apologize for not having treated the subject assigned to me in this "symposium" in a clinical fashion.

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[14] *Yearbook of the Department of Agriculture,* 1907, p. 375.

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THE ÆTIOLOGY OF PELLAGRA.*

By C. H. Lavinder, M. D.;
Washington, D. C.,
Passed Assistant Surgeon, U. S. Public Health and Marine Hospital Service.

(*Published under the Imprimatur of the American Society of Tropical Medicine.*)

Pellagra has become of interest to American medical men only since 1906, and even now it is of practical importance chiefly to only one section of our country. Its appearance, however, as experience in other countries has amply demonstrated, is a matter of much gravity, and the question may in time assume the proportions of a national calamity.

A disease of this endemic epidemic type is naturally of great interest to me as an officer of a national public health service, and of course my more direct interest would, for like reason, lie in the direction of its ætiology and epidemiology. Our experience with the disease in America has not been extensive, and our literature, though rapidly increasing, is as yet of small volume. It is my purpose in this paper then to attempt only a brief, general review of what is known regarding its ætiology.

The ætiology of pellagra, in any definite, scientific sense, is essentially unknown. In the words of a recent Italian writer: "The actual knowledge of the cause and nature of pellagra, one may say, remains still in the realm of hypothesis, although an extraordinary scientific activity on the part of students, especially Italian students, has thrown light on many

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important points." In spite of this fact, however, even a brief review of the extensive literature will soon convince one that profound convictions are held as to its nature and cause by the vast majority of students of this interesting disease.

The very early views entertained as to the nature and cause of pellagra, such as its being an atypical expression of leprosy or of syphilis or of scurvy, while interesting, possess now perhaps only historic value. For, with the exception of a small group of students, to whom I shall later refer, no doubt is expressed that the disease is a distinct entity with its own peculiar morbid phenomena. Indeed its unique symptomatology, its anatomical lesions, epidemiology, and geographical distribution would seem to leave no doubt upon this point.

With regard to the cause of pellagra, throughout all of its literature there stands one supreme idea or theory, which permeates almost all authors, directs most research work, and upon which is founded practically all attempts at its restriction or eradication. This idea is the ætiological relation declared to exist between pellagra and the extensive use of maize, or Indian corn, as an article of food. This idea seems to have arisen very early in the history of the disease, and such a suspicion may possibly even have been entertained by Casal himself[1], who is credited with first having described pellagra. Indeed there are authors who are inclined to maintain that pellagra was known before Casal's day, and that even then suspicion had fallen upon maize as its cause. At any rate, the idea, in a vague sort of way, was an early and persistent one. It was perhaps first formulated, early in the nineteenth century, by Marzari, who believed that maize caused the disease by reason of its deficiency in certain nutritive qualities. Thus later came into tangible existence the great maize theory of pellagra, and the final creation of the so called "zeist" (from *Zea mays*) and "antizeist" schools of thought. The maize idea, in one form or another, has ever since held a dominant place in the ætiology of pellagra.

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[1] Arnould, J. In *Dictionnaire encyclopédique des sciences médicales*, p. 316. "D'ailleurs Casal entrevit aussi l'étiologie; il pense *ab utrisque, atmosphæra et cibis, exurgere totalem ipsius morbi causam.*"

Following its definite enunciation, the maize doctrine, more or less rapidly, began to undergo a development and modification which has continued up to the present time, with a consequent almost bewildering variety of opinions.

The first important step in its evolution was the announcement of Balardini's "verderâme" theory. This observer had noticed on the grain a greenish discoloration, shown later to be a growth of *sporosorium maydis,* and he conceived the disease to be due to this hyphomycete. This introduced a new phase of the maize idea in attributing the disease, not to maize *per se,* but to spoiled or damaged maize. Largely through the labors of Lombroso, who was doubtless stimulated by Balardini's conception, this idea was later developed broadly, and so ultimately came into existence what is sometimes called the "zeitoxic" school, who maintain that not in maize, but in spoiled maize (*i. e.,* maize which under the influence of bacterial growth has undergone some change) must the cause of pellagra be sought.

It seems unnecessary to trace step by step the evolution of the maize doctrine, and it will, perhaps, serve every purpose to state briefly the present views held by various writers on this subject. But before doing so it may perhaps be more logical to state, with equal brevity, the general grounds upon which are based an ætiological relation between maize and pellagra. The broad statements may be given, as follows:

1. It is declared that history and observation show clearly that the first appearance of pellagra, and its later dissemination, followed, more or less closely, the introduction of maize culture into Spain and its gradual spread to France, Italy, and other countries of southern Europe.

2. It is declared that pellagra is found as an endemic disease only in those countries where maize is grown and extensively used as an article of diet by the poorer rural classes. It is of importance to note on the other hand that the area in which pellagra is found endemic is but as a spot on the extensive area over which maize is found under cultivation. There are vast tracts where maize is, and has been grown and used as food for many years, and yet no pellagra has appeared. This is a matter of much import with regard to the ætiological rôle which spoiled maize is supposed to play.

3. It is declared that countries in which maize is not grown or used as food, or only exceptionally so used, even though contiguous to pellagrous sections, or actually surrounded by them, are free of pellagra. There are numerous striking instances of this kind reported in the literature of pellagra (see Lombroso, Procopiu, Babes and Sion, and others).

4. It is declared that a change of food either among individuals, or groups of individuals, brings constantly a diminution or disappearance of pellagra, or *vice versa.* There are also many reported instances of this kind. Most writers allege that recovery may take place, or amelioration occur in the condition of pellagrins by removing from their diet all maize and maize products. The case of Corfu, in this connection, is regarded as such a notable instance that it may bear quoting. Typaldos states

that pellagra was unknown in this island previous to 1857 and that up to that time the inhabitants grew their own maize, which was of a fine quality, but, for economic reasons, the culture of grapes became almost universal, and they began to subsist on an imported maize of very poor quality, that is spoiled maize. Pellagra followed and became endemic, and he found in 1866 eighty-one cases there. (Arnould.)

Now to return to the various modifications of the maize theory, if we disregard some of the finer distinctions, they may perhaps be grouped as follows:

1. The idea that maize, as a food stuff, is wanting in proper nutritive value. This conception is in reality no longer held, having been rather effectually discredited by many careful analyses of maize which show that this cereal possesses high nutritive value, is rich in fats and nitrogenous substances, and is easily assimilable. In food value it compares very favorably with rice, for example, which constitutes a staple article of diet among a numerous class of people who do not suffer from pellagra. Pellagra is moreover not infrequently found among well nourished individuals, and its symptomatology is not that of inanition.

2. The idea that good, sound maize contains certain toxic substances which cause pellagra. This is another view which has been largely discredited by the absence of pellagra in so many places where maize is, and has been, for long periods, extensively used as food.

It is also worth while to note that the gross distinction between sound and spoiled maize is, in the opinion of many able observers, not always easily determined. Maize, by reason of its high fat and nitrogen content, seems quite subject to change under the influence of bacterial growth, and grain which to all appearance may seem perfectly sound can nevertheless be shown to be spoiled or damaged to a greater or less extent.

3. The toxicochemical idea that under the influence of parasitic growths (bacteria or moulds) maize may undergo certain changes with the formation of one or more toxic substances of a chemical nature (exogenous poisons). This idea has a host of adherents. It was established through the admirable labors of Lombroso who has been its great advocate and exponent; and it is perhaps today the most popular of all the various phases of the maize theory. It is not without critics and antagonists however, and Lombroso's experimental work and conclusions have been seriously called in question by many able students of the disease.

Lombroso, after devoting more than a quarter of a century to the problem, came to the conclusion that certain toxic substances are produced in the maize by the growth of saprophytes on the grain, and that the use of such maize as food produced pellagra. He failed directly to incriminate any particular microorganism. In investigating chemically the poisons in question, he describes three substances, a red oil, a highly toxic substance or "pellagrozeina," and a resinous substance. "Pellagrozeina" he found the most toxic of all these substances, and in its action on animals very similar to the poisonous materials held responsible for the production of ergotism. It is probably not a definite substance and has been said to contain at least two active principles, one tetanizing (like strychnine), the other narcotic (like conium). In animals inoculated with these toxic substances Lombroso noted such symptoms as wasting, muscular spasms, diarrhœa, and death; in fowls loss of feathers also occurred. He also gave a tincture of spoiled maize to men and observed changes in appetite, some loss of weight, erythemas, desquamation, and other skin lesions, with sometimes light diarrhœa.

In the opinion of many such acute lesions are not comparable to pellagra, and similar conditions may be produced with other harmless cereals submitted to the same process.

A great number of students have accepted Lombroso's ideas in general and followed him in this field, seeking principally to determine the character of the toxic substances produced and the microorganisms responsible for them. Erba, Hausemann, Pellogio, Gosio and Ferrati, Mariani, Belmondo, Pelizzi, Tirelli, Babes and Sion, and many others have obtained various toxic substances from spoiled maize, but so far there is not sufficient evidence to call any of these substances specific in their nature. The evidence submitted seems only to show that from spoiled maize various poisonous substances may be obtained which in animals, and even in man, will produce symptoms or changes which appear somewhat like pellagra. On the other hand, it is known that extracts from other grains, similarly spoiled, may likewise contain similar poisonous properties.

It is of much interest in this connection to know that Babes and Manicatide succeeded in neutralizing the toxicity of spoiled maize extracts with the serum of cured pellagrins; and, from a series of carefully conducted experiments, concluded that the blood of pellagrins contains a substance which possesses the property of counteracting the toxic action of the extracts of spoiled maize.

4. The toxicoinfective idea that from spoiled maize there is formed within the body certain toxic substances (endogenous).

Neusser advocated the view that under some circumstances there is formed in maize, largely under the influence of the *Bacterium maydis,* a certain "receptive mother substance" which later, in the body, underwent a further change. Under other circumstances, however, he viewed the disease as a direct intoxication.

De Giaxa, following an earlier idea of Di Donna's, attributed great importance to the action of the colon bacillus on ingested maize. His idea seems to have been that the vegetating properties of this bacillus may become greatly modified on a culture medium of maize, and he alleges that he has shown the production, by the colon bacillus on maize media, of specific toxic substances.

Marie also seems to favor the conception of an autointoxication. After reviewing, with approval, Pelizzi's work, he seems to think it reasonable to suppose that the necessary elements in the production of pellagrous symptoms, once in the blood, may decompose there under the action of certain bacterial ferments ingested with the maize, and undergo toxic transformations. He thinks the toxic substances involved may perhaps be more nearly related to amorphous chemical ferments, and suggests that the pellagrous poison may be polytoxic.

5. The idea that pellagra is a specific infection, derived from maize, either a mould or a bacterium.

The flora of maize has been frequently studied, and a great number of parasites named and described. Most of these, however, have attracted little attention with the exception of the fact that all may cause changes in the grain upon which they vegetate.

Following Balardini's *sporosium maydis,* which was later discredited, Pari incriminated the maize smut (*ustilago maydis*). This, too, was discredited.

In 1881 Majocchi discovered on maize a motile organism which he called *Bacterium maydis.* He asserted also to have found it in the blood of pellagrins. Cuboni later found a similar microorganism in spoiled maize and in the stools of both healthy persons and pellagrins, but in greater profusion in the latter. Paltauf and Heider and others worked with this microorganism, and it was later shown to be the ordinary potato bacillus.

In 1896 Carrarioli reported that he had found a bacillus in the blood and stools of pellagrins, which he named *Bacillus pellagræ.* His results have not been confirmed.

In 1902 Ceni declared pellagra to be due to an infection by two moulds, *Aspergillus fumigatus* and *flavescens*—a true aspergillosis. He states that the spores of the aspergilli, ingested with food, escape through the intestine and locate in the lungs, pleuræ, pericardium, and pia mater, from which places he has been able to isolate them at autopsy. He also states that the greatest toxicity of the aspergilli occur at that season when pellagrous symptoms are most in evidence, and that this corresponds to the "cycle of the annual biological evolution" of these hyphomycetes. Later, with Besta, he found these moulds to possess a virulent and characteristic toxine, which resides almost exclusively in the spores, and determined that the media on which they grow plays but little part in its production. More recently Ceni and Besta are said to have found toxic properties in *Penicillium glaucum.*

Tizzoni, in a series of recent papers, announces the discovery of a specific microorganism, which he calls *Streptobacillus pellagræ.* This work has, of course, not been confirmed. In his first paper (1906), working with Fasoli, he states he isolated from the blood and organs of acute pellagrins (*tifo pellagroso* and *frenosi pellagrosa*) a bacillus which he found pathogenic for the usual laboratory animals, and which in the guinea pig produced a very suggestive clinical picture and anotomical lesions. In his next paper, working with Panichi (1907), he experimented with rabbits and guinea pigs by introducing into the stomach cultures of this same bacillus. From these experiments he concluded that this bacillus had an elective action upon the intestine of any animal, but in the more susceptible guinea pig it produced death with an experimental and anatomical picture similar in all respects to pellagra, provided the diet of the animal contained a liberal share of maize. In his last paper (1909) he reviews his previous work, announces the isolation of the same microorganism from the stools and blood of chronic pellagrins as well as from spoiled maize. He describes two distinct strains of this bacillus, easily distinguished, and thinks these strains correspond to different grades of virulence (acute and chronic pellagra), that the symptoms and anatomical lesions produced in the guinea pig correspond to those of pellagra, that the elective lesion is in the intestine which is always primarily involved, that this intestinal lesion is always followed by a specific, general intoxication, especially manifested upon the nervous system, blood vessels, and red cells, and secondarily upon the liver and kidneys; finally that these toxines show a long period of latency, and have a particular affinity for the nervous system, conducing ultimately to its profound disintegration.

So much for the maize theory and its variations. Now when we turn to the "antizeists" we find them greatly in the minority. There are two great facts which have been urged against the maize theory. First, and most significant, is the extensive territory over which maize is and has been cultivated and used as food for many generations, and yet no pellagra has appeared. The second is the frequently reported cases of pellagra in which there is no history of the use of maize or its products by the sufferers as food.

The first statement is of course evident, and the "zeitoxic" idea is offered in explanation. The second is by no means always admitted, and has proved the cause of much controversy. Soon after its creation the "zeist" idea met with much opposition, and later a group of French thinkers, especially Landouzy and others, reported a number of cases of pellagra where no maize had been consumed. Roussel, the able and ardent French "zeist," sharply questioned such observations and rather effectually discredited the diagnosis, introducing at the same time into the literature of pellagra the now well known term pseudopellagra, which he thought described their cases, as they did not conform to the picture of the true disease. This term, pseudopellagra, has itself been the cause of confusion to some and an object of ridicule to others. Manson speaks of the invention of the comfortable term pseudopellagra, and scornfully remarks: "The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize, but when this is not possible, the disease becomes pseudopellagra."

From France frequent reports have been and are being made of pellagra without maize, and there has grown up there a school of thought which denies that pellagra is a morbid entity at all. It is spoken of as the pellagrous syndrome and regarded as a *morbus miseriæ* (see Cecconi, Le Fers, and others). It is undoubtedly true that there may arise among alcoholics and in cachectic states, especially among the insane, certain symptoms simulating in many respects pellagra, yet such a diagnosis is not admissible; and it is said that a careful study of such cases readily permits discrimination. Certainly it seems difficult to understand how doubt can arise that pellagra is a disease *sui generis,* when consideration is given to its unique symptomatology, its anatomical lesions, epidemiology, and geographical distribution.

All criticism of the maize school, however, is not of this destructive type. At the meeting of the British Medical Association in 1905, Sambon, in a remarkable paper, put forward the highly interesting suggestion that pellagra might be due to some protozoon, a suggestion which has later met with the hearty approval of Manson. The general line of this argument is that an examination of the numerous observations and experiments shows one fact clearly, and that is that each investigator asserts that he has reproduced pellagra, either in man or animals, and yet it is evident that the disease can have but one cause. It is unwise, therefore, to place too much reliance on such experiments, and it should not be forgotten, as history amply shows, that the interpretation of experiments is often as fallacious as the interpretation of natural facts. The reputed historical facts with regard to the relation between the introduction of maize culture and the appearance of pellagra are called in question, and an attempt is made to. show that there is historical evidence to prove that maize was grown in Europe long before the date usually assigned. It is pointed out that the areas of maize growing and pellagra endemicity do not coincide, that pellagra has been observed frequently in parts of France, Spain, and Italy where maize is not cultivated, and that the comparative study of the distribution and prevalence of pellagra at different periods is decidedly unfavorable to the maize theory.

The opinion is expressed that the prevailing ideas as to the ætiology of pellagra are very unsatisfactory, and that the maize idea has been much too dogmatically adhered to by investigators. The suggestion is made that pellagra shows many analogies with such diseases as syphilis, trypanosomiasis, and kala azar. Such remarkable resemblances are noted between pellagra and trypanosomiasis as the characteristic, perivascular, small cell infiltration, benefit by treatment with arsenical preparations, and the mononuclear increase in the blood. It is further suggested that the parasite may be insect borne, and the erythema of pellagra may be one of those interesting instances of correlation in nature whereby the parasite is enabled to enter some intermediate host, complete its life cycle, and perpetuate its existence, such as is seen in the correlation between the night swarming of the larvæ of certain filaria and the nocturnal habits of its intermediate host, the mosquito; and that maize may perhaps be found to sustain some such relation to the ætiology of pellagra as the swamp has been shown to sustain to the ætiology of malaria.

In this connection it is highly interesting to record that Babes and others in a very recent article have reported highly beneficial effects in the treatment of pellagra by atoxyl and arsenous acid combined, and they have put forward practically the same suggestive idea as Sambon's. They state that the almost specific therapeutic action of arsenical preparations as well on certain protozoal diseases as upon the manifestations of pellagra at least suggests, by analogy, some conclusions as to a similar ætiology. Pellagra, they still think, is in all likelihood due to some change in maize caused by parasitic influence, and the idea can not yet be excluded that from spoiled maize not only toxic substances but parasites as well may be conveyed to the predisposed human organism, either direct or by means of insects or other organisms.

From its analogy to malaria, piroplasmosis, and trypanosomiasis, diseases to a certain extent with the same geographical distribution, the thought is justified that for the transmission of pellagra some similar, intermediate, animal host is necessary; and for the intoxication or infection itself some microscopic animal parasite. Such a parasite must necessarily be very small, perhaps ultramicroscopic, and, although in their researches they found only in the erythematous skin of pellagrins bodies resembling the smallest Negri bodies, yet the results of arsenical treatment encourage new investigations along the lines suggested.

The usually given *predisposing causes* of pellagra contain some facts worthy of brief mention.

With regard to *age* the statements are somewhat discordant, but it is worthy of note that the disease does not occur in infants and seems to be rare in children. The usual age seems to be about twenty to forty.

Its relation to the *seasons and sun,* from the characteristic, spring erythema has furnished much cause for discussion at times; and the disease has been called the "sun disease," "sunstroke of the skin," etc. General opinion, however, seems to attribute to the sun only a mild, exciting effect in the production of the erythema.

Alcoholism and other depressing conditions exert only the indirect influence of lowering resistance, but it should be noted that the toxic substances of spoiled maize are soluble in alcohol and hence alcohol may contain such poisons.

From a review of the literature one would seem justified, at least tentatively, in making the following statements:

That the cause of pellagra is essentially unknown.

That the idea, in one form or another, of an ætiological relation between pellagra and the use of maize as food, is held by the majority of students of the disease, that such an idea is almost as old as the history of the disease itself, that it rests to some extent upon the observations and experimental work of many able men, and that, in consequence, it is not to be lightly cast aside, though, at the same time, it would seem unwise to hold such views so dogmatically as to exclude investigation along other suggestive lines.

That Ceni's work on the direct infection by certain hyphomycetes (aspergilli), and Tizzoni's work on his specific *Streptobacillus pellagræ,* while well worthy of serious attention at the hands of investigators, remain yet to be confirmed.

That Sambon's suggestion of the possible protozoal nature of the disease rests largely on an argument by analogy, and is at present little more than a suggestion, though an extremely interesting one. It offers a new, and possibly profitable, field for investigators.

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Discussion.

Dr. George Dock said that from Dr. Alsberg's remarks one might get the idea that pellagra had developed in the United States on account of the change of conditions for the raising and selling of corn. Some believed this, but others thought that the disease had existed before but had been overlooked. Dr. Dock had heard of cases in the South that had occurred before the existence of those changed conditions, and he strongly suspected that he himself had seen a case in Texas. At the time he had taken it to be a dermatitis. He considered it a matter of minor importance, however, whether it existed years ago or not. The main point was that it existed now, and in a form difficult to recognize and undoubtedly very often mistaken. When one reallized how absolutely uncinariasis had been overlooked for a long time, one would readily admit that the same might occur with pellagra. Therefore a great extension of clinical knowledge regarding the latter disease was needed.

Dr. Dock then referred to a typical case of pellagra and one less typical that he had seen in a hospital in Atlanta, and to three suspected cases that he had since examined in New Orleans. In one of the latter there was a quite characteristic dermatitis, with rough skin, discoloration, etc. In another of these cases the symptoms were also very suspicious, but in none was there any alteration in the mucous membranes or marked gastrointestinal disturbances. The clinical recognition of the disease was difficult in the less marked cases, so that anything that the

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members of the society or the general government could do in sending out circulars and clear descriptions of the clinical conditions and modes of advance in pellagra ought to do a good deal of good.

Dr. J. M. ANDERS, of Philadelphia, said that he had received a note from Dr. Theodore C. Merrill, of Colorado, Texas, inclosing a report on pellagra for the State of Texas, which he wished to read. The note was as follows:—

"The result of recent investigation concerning Texan pellagra may very well be stated in the phrase 'There isn't any.' Inquiry sent to the various State institutions and army posts within the State reveals not a single recorded case for the years 1898-1908 inclusive. Dr. M. L. Graves, professor of medicine in the State University Medical Department, writes me that he has been on the lookout for the disease for several years, but has not yet seen a case. Questions addressed to various medical men throughout the State fail to bring to light either epidemics, endemic outbreaks, or isolated cases. Some time ago I reported a case diagnosticated as pellagra in the *Journal of the American Medical Association.* I cannot give the date of its publication, but it is easily to be found. I trust I was duly cautious, but as I took great care in describing the symptomatology present, and also had an examination thoroughly made of suspected corn meal, it may be that my case was really one of pellagra. From *economic* reasons it is very gratifying to have only general absence of this disease to report for this State. If at any time I may be able to discover any obscure pellagralike epidemics, I shall try to investigate them carefully."

Dr. ANDERS called attention to the fact that, of 196 cases of pellagra collected by Wood, seventy had occurred in North Carolina. This suggested the probable influence of locality as a predisposing factor. Dr. Anders referred to an acute form of pellagra prevalent in the southern States, which proved fatal in from four or five weeks to three months, this form being unknown in Italy. The average duration of cases in the United States, even in the chronic form, was only three years, whereas it was at least five years in Europe. Therefore, racial influences apart, the marked influence of locality, including possible climatic conditions, must be taken into account in any attempt to solve the problem of the ætiology of this disease. He did not mean to imply that the conditions in the two countries were different, but that there was a more acute manifestation or development in these United States.

Dr. Edward R. Stitt, of Washington, related a conversation that he had had five years before with Dr. Sandwith concerning the existence of pellagra in the United States. Dr. Stitt said: "It seems strange that we have no pellagra in the United States when one considers that this is a great maize eating country." Dr. Sandwith replied: "You have not the poverty in the United States that they have in Italy and Egypt." "There is a great deal of poverty in the South," responded Dr. Stitt. "Well," said Dr. Sandwith, "your maize is good." "I beg to differ with you again," said Dr. Stitt. "There is a good deal of spoiled corn meal eaten there." Dr. Sandwith absolutely maintained that the aspergillus was the cause of the disease. Dr. Stitt said that he did not know what the cause was, but that the corn was just covered with mould. "Ah!" said Dr. Sandwith, "but have you no pellagra in the United States? I am sure that I have seen two cases there." Dr. Sandwith also suggested that it would be a good plan to have American physicians see cases of pellagra in Egypt, where the disease occurred in its most typical form. Dr. Stitt visited the Kaisr el Ainy Hospital in Cairo in the month of August and saw seven cases in the wards. Dr. Phillips was showing these cases to him. At each case they came to Dr. Stitt would say: "I should not be able to see anything in that case"; and Dr. Phillips would reply: "There is not much to see in it now, but there would have been, if you had seen it in April or May. In these months the cases of pellagra show certain symptoms that have disappeared by August." In not a single one of the seven cases shown Dr. Stitt as pellagra could he see any typical symptoms. Dr. Phillips said that there were tremors and other things of that sort present, but no other symptoms.

Dr. William S. Thayer, of Baltimore, referred to a case that he had seen in 1905, which presented a typical picture in many respects. The patient was the sister of a physician living not far from Baltimore. She had had two previous similar attacks, associated with diarrhœa, an eruption on the backs of the wrists, and marked stomatitis. The condition lasted a month or so, and then cleared up. Dr. Thayer happened to have been reading an article on pellagra the day before he was called to see this patient, or he would not have recognized it. The skin on the backs of the hands was discolored with crusts, exactly like the pictures he had seen of pellagrous changes. The patient was in a dull, drowsy, stupid mental condition, and would not answer questions. She had evidently had some delusions, and the whole picture was like that of pellagra. There was no change in the reflexes, but she had a peculiar puffiness under the eyes. Something about her appearance suggested myxœdema to Dr. Thayer, though there was no particular swelling in any other part of the body. He could not feel any thyreoid swelling. The patient was put upon thyreoid extract, with immediate recovery, and no relapse. Dr. Thayer had often wondered whether this could have been a case of pellagra, after all. In that case, he thought it would be worth while to investigate whether thyreoids would not do good in that disease.

Dr. Thayer said that the action of arsenic in pellagra was remarkable. Intensive arsenical treatment had produced some very good results in trypanosomiasis. Therefore it was worth while to try its effect in pellagra. In a reported case, on two successive days seven grains of atoxyl were administered hypodermically, and seventy-five grains of an ointment containing arsenous acid, 1 to 5, were rubbed in. Several pills of arsenous acid were also administered. If necessary, this treatment should be repeated on two successive days a week later. Forty cases were reported, several of them being obstinate. In many of these there was a prompt recovery, and it was unnecessary to give the treatment a week later. Dr. Thayer considered this result so remarkable that he could not help feeling skeptical regarding it.

Dr. THOMAS B. FUTCHER, of Baltimore, asked whether it was known how long a person must be subjected to the infection in order to acquire the disease. He wished to know whether eating one meal of infected maize would produce it, or whether it was necessary for an individual to be subjected for a long time to the toxine or germ.

Dr. ALSBERG said that he did not think that there were any exact data regarding this point. In Italy the disease broke out in the spring, and seemed to be connected with the open air life and the hard work done by the person. In Egypt it occurred in the spring and in the fall. There was a small occurrence in the fall in Italy also. In regard to the difference between pellagra here and in Europe, Dr. Alsberg was not sure that there was any real difference. He had seen cases of pellagra some years ago in Italy in the spring; but, unfortunately, he was not then interested in that disease, and did not imagine that he would ever have anything to do with such cases. His impression, however, was that the early cases were very slight indeed, and that one mild spring attack was followed by a severe one the next spring. He believed that it would probably require three years before a case would require serious attention. He thought that a good many of the early cases were overlooked in this country, especially in colored persons. He had not had much experience in treating colored people, but he thought it would be difficult to discover an erythema on their skins; and one would expect most cases of pellagra in the country to be in colored people.

Dr. Lavinder said that he had done some work with Dr. Wood. It seemed to him, however, that not enough reports had been received from men who had seen the disease clinically to enable one to draw conclusions. The mortality from measles among us was not very high, but, if introduced into a virgin population, it would be an exceedingly fatal disease. Even if pellagra was a food poisoning, one might expect the same thing to be true of it. While the Italians did have an acute pellagra, what they meant by this term was an acute exacerbation of a chronic case. He suggested that it would be well to adopt one pronunciation for the word pellagra, as four different ways of pronouncing it had been heard during the afternoon.

THE PREVALENCE AND IMPORTANCE OF UNCINARIASIS AMONG APPARENTLY HEALTHY SOUTHERN-BRED WHITE MEN IN THE UNITED STATES ARMY *

WESTON P. CHAMBERLAIN, M.D.
JACKSON BARRACKS, LA.

Until very recently the prevalence of hookworm disease among soldiers who have always resided in the United States appears to have been very little investigated. The only mention of uncinariasis in the report of the Surgeon-General of the Army for 1908 is that an examination of the stools of 21 soldiers at Fort Root, who had recently returned from the Philippine Islands, showed all to contain ova of *Ankylostoma duodenale.* In 1904 the surgeon at Fort Porter, New York, reported the presence of ankylostoma in many cases admitted to hospital for other conditions; but where the infection probably originated is not stated in the reference to his work. On Dec. 7, 1908, Captain J. F. Siler, of the Medical Corps of the Army, stationed at the large recruit depot of Fort Slocum, New York, reported to the Surgeon-General that of 19 southern recruits examined, 16, or 84 per cent., harbored ankylostoma. Of these, 3 were suspected of being so infected, while the remainder were in hospital for other reasons.

As a result of Dr. Siler's work, instructions were sent out for army surgeons to investigate the prevalence of uncinariasis among southern-bred soldiers.[1] The result of my work on this subject illustrates how a well-known condition may be entirely overlooked until one's mind is specially directed to it. Prior to the present investigation, no case of uncinariasis had ever been recorded on the sick report at Jackson Barracks. During the three years I have been stationed there two cases were suspected of ankylostomiasis, but on examination both proved negative. Yet the result of my recent work is to show that 25 per cent. of the entire command harbored the hookworm, and that the condition had been wholly unsuspected. It is undoubtedly true that similar mild infections are being constantly overlooked throughout the southern states as well as in the army.

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*Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10, 1909.

[1] By "southern-bred" is meant in this article men who were born and always had lived in some one of the following states: Maryland, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Texas, Kentucky, Tennessee, Arkansas and Missouri.

PERCENTAGE OF MEN INFECTED

The work at Jackson Barracks has consisted of the examination of the blood and stools of 147 apparently healthy soldiers. For analysis these 147 cases are separated into four classes. The details are given in appended tables.

Class 1.—Newly enlisted southern-bred recruits received at the recruit depot at Jackson Barracks. There were 43 of these, and 29 were infected with uncinaria, a percentage of 67 (Table 1).

Class 2.—Southern-bred soldiers in the permanent command at Jackson Barracks serving in their first enlistment; that is, having three years or less in the army. Fifty-seven of these were examined and 31 were found infected, a percentage of 54. The average length of service for these men was 1.1 years, and only a single one of the positive cases had been in the army over two years (Table 2).

Class 3.—Southern-bred soldiers in the permanent command at Jackson Barracks who have served more than one enlistment; that is, over three years. There were 33 of these examined, and only 4 were found to have uncinariasis, a percentage of 11. The average length of service for these men was 6.4 years. The four men infected had served, respectively, 4, 5, 6½ and 7 years. The number of worms found in these cases was small, the average being 5½ per man (Table 3).

Class 4.—Soldiers and recruits at Jackson Barracks who had lived little or not at all in the south. Fourteen of these were examined, and no ova of uncinaria were found nor did the eosinophile count of any suggest the presence of intestinal parasites.

If the new recruits (Class 1) and the soldiers in their first enlistment (Class 2) are combined, we have 100 southern-bred soldiers with less than three years' service among them among whom an even 60 per cent. were infected with hookworms. Adding the 4 positive cases among the older soldiers, gives in all 64 cases of uncinariasis to be studied.

That this high percentage of uncinaria infections among southern-bred recruits is probably the rule rather than the exception is shown by the following reports: Captain P. J. Owen, Medical Corps, U. S. A., stationed at Columbus Barracks, Ohio, records the finding of 8 cases of infection with *Uncinaria americana* among southern recruits, though how many were examined in all is not stated. Captain Siler has recently written me that he has now examined 140 recruits, finding over 85 per cent. infected. My own work in this direction was brought to an unexpected conclusion because of the sudden cessation of recruiting in New Orleans made necessary by reason of the fact that the army had nearly reached its authorized strength.

Strong reports[2] that in an investigation of 4,106 Filipino prisoners 52 per cent. were found to be infected with uncinaria. If this can be taken as an index for the general population of the Philippines, it appears that the proportion of infections among the Filipinos, living in their insanitary manner, is not as high as that of southern-bred recruits who probably are less likely to be infected than the mass of the rural population of the south.

CLINICAL SIGNS OF LIGHT INFECTIONS

First of all, it must be clearly understood that none of these infected subjects studied by me were sick. Many never had been on sick report, and, of those who had, only one presented symptoms which, in the light of positive uncinaria findings, could be attributed to the parasites. This patient had been in hospital several times with slight fever, indefinite intestinal symptoms and fleeting pains in chest and abdomen. He was unable to do any heavy work without soon becoming used up. Hemoglobin was 80 per cent. Seventy-seven worms were obtained after he was treated. With this exception, the cases I am reporting belong to the class of which Stiles says: "Under light infections may be included those patients who show eggs in the feces on microscopic examination, but who do not exhibit any or sufficiently marked symptoms to attract special attention. These cases are numerous and important, as they are capable of keeping a region infected and thus giving rise to severe cases. Hence from a prophylactic standpoint they should always be treated when found." That these cases can not be detected by mere inspection is evidenced by the words of Stiles, that "if these light cases were submitted to physical examination for enlistment in the army or navy, probably most of them would be accepted as sound."

As will be seen in the appended tables, I have classed the color of the men examined as "excellent," "good," "fair" or "pale." By "excellent" is meant the fresh, ruddy complexion so common among healthy northern men. It will be observed that very few of the southern men possessed this "excellent" color. Many are recorded as fair and a few as pale, but there

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[2] Strong (R. P.): Combating tropical diseases in the Philippines by scientific methods. Jour. Am. Med. Assn., 1909, lii, 524.

TABLE I.—FORTY-THREE UNSELECTED SOUTHERN-BRED RECRUITS EXAMINED AT JACKSON BARRACKS, LA.*

Case No.	Age.	Height, inches.	Weight before treatment.	Weight after treatment.	Occupation at time of enlistment.	Occupation previous to enlistment.	Birthplace.	Residence.	History of ground itch.	Years since ground itch.	Color.	% hemoglobin	% Polynuclears.	% eosinophiles.	% lymphocytes, small	% lymphocytes, large.	% transitionals.	% mast cells.	Number of ova found in stool.	Number of worms found after treatment.	Remarks.
1	22	66	124	133	Farmer	Farmer	Miss	Miss	N	....	Good	100	62	6.5	22	7	2.5	0	Many	18	
2	21	68	133	140	Farmer	Farmer	Miss	Miss	P	12	Good	100	66.5	8.5	16.5	5.5	2	1	Many	42	
3	23	69	135	135	Plumber	None	S. C.	Ala	P	14	Pale	80	74.5	2	15	3.5	5	0	Few	0	
4	18	66	127	124	Factory	Farmer	Miss	N. C.	P	14	Good	100	44	26	22	4	4	0	Few	3	
5	24	68	145	152	Farmer	Farmer	Miss	Miss	P	14	Pale	80	46	7	26	11.5	9.5	0	Few	17	
6	21	69	127	....	Solicitor	Engineer	Ala	Ala	N	....	....	....	35.5	7	44.5	9	3.5	0.5	0	......	Never lived in country.
7	19	66	118	....	Laborer	Laborer	Miss	Miss	?	....	Good	90	40	20.5	25.5	4	5	0	Very few	......	Left before treatment.
8	23	68	128	129	Collector	Farmer	Ga.	La.	P	15	Good	90	60.5	7.5	20	7	4.5	0.5	....	33	Farmer 6 years ago.
9	20	66	126	129	Lumber	Farmer	Tex.	Miss		9	Good	90	63	11	17	6	3	0	Many	10	
10	28	68	153	159	Engineer	Farmer	Ala	Miss	P	20	Good	80	47	8.5	32	7	5.5	0	Very few	2	Farmer 6 years ago.
11	22	69	144	154	Farmer	Farmer	Ala	Ala	P	12	Fair	80	69	7	15.5	4	3.5	1	Very many	12	
12	27	66	130	....	Carpenter	Farmer	Miss	Miss	P	18	Pale	90	62.5	15	9.5	3.5	9	0.5	Few	5	
13	23	65	128	....	Sawmill	Farmer	Miss	Miss	N	....	Good	90	65	1.5	20	8.5	4.5	0.5	0	......	Not on farm for 11 years.
14	23	72	151	....	Barber	Farmer	Fla	La.	P	7	Fair	80	51.5	17	23	2.5	5	1	Very many	......	Left before treatment.
15	18	67	150	159	Laborer	Farmer	W. Va.	La.	N	....	Pale	90	49	11	28.5	5.5	5	1	Very few	0	
16	26	67	129	139	Laborer	Farmer	Ala	Ala	P	20	Good	90	68	5	23	2.5	1.5	0	Few	1	
17	29	69	152	....	Factory	Farmer	Ala	Ala	P	5	Pale	90	71.5	4.5	18	3	2	1	Few	......	Left before treatment.
18	23	72	150	154	Farmer	Farmer	Ga.	Ga.	P	15	Good	80	65	10.5	14	3.5	6.5	0.5	Very many	0	
19	31	70	190	....	Carpenter	Butcher	Ga.	Ga.	P	4	Good	100	56	2.5	34.5	4.5	2.5	0	0	......	
20	23	72	147	157	Stable	Farmer	Ala	Ala	P	12	Pale	100	68	4	20	6	2	0	Very many	2	
21	25	65	124	....	Cooper	Farmer	La.	La.	P	15	Good	100	50	2	39.5	5.5	3	0	0	......	

22	21	64	126	126	Machinist.....	Farmer........	La.....	La.....	P	12	Good...	100	58.5	5.5	29	4.5	2.5	0	Very few	16	
23	22	70	152	147	Machinist.....	Farmer........	N. C...	Pana...	N	....	Xlnt...	100	60	7	25	5	2	1	Many....	1	
24	24	69	133	....	Showman	Farmer........	Pa.....	Ala	N	....	Fair...	90	75	2	17	4	2	0	0	......	Not on farm for 12 years.
25	27	71	150	149	Laborer.......	Farmer........	Tex....	Tex....	N	....	Good ..	90	31	5	50	7.5	6.5	0	Many....	24	
26	21	69	157	159	Farmer........	Logging.......	Miss...	Miss...	P	8	Good...	100	68.5	8.5	16.5	3.5	2.5	0.5	Few......	1	
27	33	71	156	....	Lumberman ..	Farmer........	Tex....	Miss...	N	....	Pale...	100	75	0	18	5	2	0	0	......	
28	21	71	154	....	Millman.......	Farmer........	N. C....	Miss...	P	10	Good...	90	50	23	15	8	4	0	Few......	......	Left before treatment.
29	21	67	140	....	Farmer	Farmer........	Miss ..	Miss...	N	....	Pale...	90	62	3	27	4	4	0	0	......	
30	22	64	122	....	Laborer.......	Millman.......	La.....	La.....	N	....	Good...	90	61	1	29	2.5	5	1.5	....	......	Never lived in country.
31	19	70	149	153	Laborer.......	Farmer........	Miss.	Miss...	N	....	Good...	90	73	6	13	5	3	0	Verymany	5	
32	23	70	157	163	Farmer........	Farmer........	La.....	La.....	N	....	Good...	90	54	26	13	3	2	2	Very few	7	
33	23	69	138	146	Farmer........	Farmer........	N. C....	N. C....	P	14	Good...	100	46	10	28	9	5	2	Few......	19	
34	18	69	125	135	Farmer........	Farmer,.......	Ala	Ala	N	....	Fair ...	90	40	10.5	35.5	8	5.5	0.5	Verymany	11	
35	21	68	129	130	Laborer.......	Farmer........	La,....	La.....	N	....	Good...	90	35.5	7	32.5	11.5	18.5	0	Verymany	75	
36	27	69	140	....	Fireman.......	Fireman	La.....	La.....	N	....	Good...	80	70	3	22.5	1.5	3	0	0	......	Never lived out of N. O., La.
37	25	69	137	....	Tinner.........	Motorman.....	La.....	La.....	N	....	Good...	....	72	0	21	4	3	0	0	......	Never lived in country.
38	29	71	150	157	Laborer.......	Laborer.......	La.....	La.....	N	....	Good...	100	56	1	36	3	3	1	0	......	Never lived out of N. O., La.
39	26	75	148	....	Carpentry.....	Farmer........	N. C....	La.....	N	....	Good...	100	49.5	4.5	39	2	4	1	0	......	
40	22	71	186	191	Pile Driver....	Teamster......	Tex....	La.....	N	....	Xlnt...	90	71.5	4.5	17	5	2	0	0	......	
41	27	67	148	141	Farmer........	Farmer........	Md	Md	N	....	Good...	90	70	6	14	4	6	0	Very few	1	
42	22	67	138	145	Showman......	Farmer........	Ky.....	Ala	N	....	Pale...	100	65	2	22	5	6	0	Very few	1	Farmed in Ky. 10 years ago.
43	28	64	120	....	Sawmill	Farmer........	Md	Ala	N	....	Good...	80	76	2	13.5	5.5	2.5	0.5	0	......	Farmed in Md. 7 years ago.

Twenty-nine cases of uncinariasis out of 43 = 67 per cent.
Average eosinophilia for positive cases, 9.9 per cent.
Average eosinophilia for negative cases, 2.4 per cent.
Average weight for positive cases, 140.2 lbs.
Average weight for negative cases, 142.9 lbs.
Average gain in weight after treatment, 3.4 lbs.

* N means negative history for ground-itch; P means positive history for ground-itch; Xlnt means "excellent."

seem to have been no notable differences in color between the positive and the negative cases.

In view of the great prevalence of uncinariasis in the South, it is thought that much caution must be used in looking on hookworms as the cause of atypical symptoms in a patient simply because the ova are found in the feces, since the presence of uncinaria in the intestines may be a mere coincidence.

TABLE III.—FOUR CASES OF UNCINARIASIS FOUND AMONG THIRTY-THREE UNSELECTED SOUTHERN-BRED SOLDIERS WHO HAVE SERVED MORE THAN ONE ENLISTMENT PERIOD (OVER THREE YEARS)*

Case No.	Age.	Years in Army.	Height, inches.	Weight before treatment.	Weight after treatment.	Occupation at time of enlistment.	Occupation previous to enlistment.	Birthplace.	Residence.	History of ground itch.	Color.	% hemoglobin.	% polynuclears.	% eosinophiles.	% lymphocytes, small,	% lymphoctyes, large.	% transitionals.	% mast cells.	Number of ova found in stool.	Number of worms found after treatment.
109	26	4	68	156	148	Farmer....	Logging...	Tenn...	Tenn...	N	Good	90	55	4	31	5	4	1	Very few	2
127	22	5	71	140	140	Machinist.	Farmer ...	N. C...	N. C....	N	Fair.	90	50	8	38	2	2	0	Many	11
129	29	6½	68	145	140	Salesman .	Farmer....	Miss...	Miss...	N	Good	90	55.5	10.5	24	4.5	5	0.5	Very few	6
132	28	7	65	156	160	Farmer....	Farmer....	Tenn...	Tenn...	N	Fair.	90	31.5	26.5	36.5	3	2.5	0	Very few	3

* Twenty-nine negative cases are omitted from table as showing nothing of interest.
N. means negative for ground-itch.
Average eosinophilia 4 positive cases, 12.5.
Average weight 4 positive cases 149.7 lbs.
Average number of worms found, 5½.

BLOOD APPEARANCES IN MILD INFECTIONS

The reduction in hemoglobin in infected men was very slight, being less marked than was found in the cases reported by Siler. No case was found with the hemoglobin lower than 80 per cent; the majority showed 90 per cent. and a considerable number 100 per cent. Among the 133 southern-bred men the average hemoglobin percentage for the infected cases was 91.5 per cent. and for the non-infected 94.2 per cent., a difference of only 2.7 per cent. No counts of red cells were made.

The leucocyte count was made in 12 infected cases, but, as it did not seem to show anything of interest, it was discontinued. The highest count was 12,700, the lowest 7,600, and the average 9,600 per cubic millimeter.

A differential count of the white cells was made in all cases and demonstrated, as was to be expected, that eosinophilia was present in the majority of those harboring hookworms. In the 64 positive cases the lowest eosinophile count was 1 per cent. and the highest 26 per cent. Fourteen cases showed less than 5 per cent. of eosinophiles. The average eosinophile count for the 64 infected cases was 8.5 per cent., and for 83

TABLE 11.—FIFTY-SEVEN UNSELECTED SOUTHERN-BRED SOLDIERS IN THEIR FIRST ENLISTMENT PERIOD (THREE YEARS) *

		Army.	inches.	before nt.	after nt.	Occupation at time of	Occupation previous to	ace.	ce.	of itch.	nce itch.		globin.	uclears.	ophiles.	hocytes, all.	hocytes, ge.	itionals.	cells.	of ova stool.	ber of s found eatment.	Remarks.
83	23	2	68	132	137	Electrician....	Electrician....	Ala ..	Ala ..	N	....	Fair...	90	24.5	13.5	51	5	5	1	Very many	38	
84	33	2	72	184	....	Lumberman ..	Farmer........	Miss.	Mo...	N	....	Fair...	100	49.5	0.5	39	5	6	0	0	......	Lived in Mo. last 13 years.
85	33	1	67	150	....	Farmer........	Farmer........	Tenn	Tex..	N	...	Good...	90	48.5	5	34	5.5	6.5	0.5	0	......	
86	23	1¼	64	123	117	Laborer.......	Laborer.......	Miss.	Miss.	N	....	Fair...	80	45.5	3.5	35	10.5	5.5	0	Very few	5	
87	28	2¼	74	175	173	Farmer........	Farmer........	Miss.	Miss.	P	10	Good...	100	35.5	7	42.5	9	5	1	Very few	15	
88	29	1½	66	139	....	Electrician....	Merchant......	La...	La...	N	....	Good...	90	65.5	0.5	16.5	9	8	0.5	0	......	Never lived in country.
89	26	1	67	142	....	Telegrapher...	Clerk..........	Tex..	Tex..	N	....	Good...	100	68	6	21	3	1	1	0	......	
90	22	2¼	69	161	....	Telegrapher...	Telegrapher...	Tenn	La...	N	....	Pale...	90	61.5	1.5	21	6.5	9	0.5	0	......	
91	24	2	67	138	....	Carpenter.....	Carpenter.....	Miss.	Miss.	N	....	Pale...	90	64.5	4.5	26	2.5	2.5	0	0	......	Lived on farm till 16 years old. Never farmed.
92	23	1½	72	163	....	Drummer	Fireman.......	La...	La...	N	....	Fair...	90	54	4	37.5	3	1	0.5	0	......	Never lived in country since 8 years old.
93	24	1½	68	137	139	Millman.......	Farmer........	Miss.	Miss.	P	10	Good...	100	38	12	47	1	1	1	Very many	24	
94	31	1	72	184	....	Farmer........	Farmer........	Miss.	Miss.	N	....	Xlnt...	100	45	3.5	36.5	11	3.5	1.5	0	......	
95	27	2	69	149	....	Clerk..........	Clerk..........	Ala .	Tenn	N	....	Good...	90	74	0	23	1	1	1	0	......	Never lived in country.
96	23	¾	65	138	136	Brakeman.....	Millhand......	N. C..	S. C.	P	15	Good...	100	62.5	3	24.5	4	6	0	Few....	10	
97	22	1¼	66	140	136	Circusman	Farmer........	Tex..	La...	N	....	Pale...	80	56	12.5	28	1.5	1	1	Few....	0	
98	32	¾	69	145	....	Machinist.....	Ironworker....	Va...	Va...	N	....	Fair...	90	61.5	5	27.5	2.5	3.5	0	0	......	Few ova tricocephalus dispar.
99	23	1¼	65	136	....	Salesman,.....	Salesman......	Ky...	La...	N	....	Good...	100	57	2	35.5	3.5	2	0	0	......	Never lived in country.
100	24	1½	70	144	....	Smith	Painter........	Va...	Ala..	N	....	Good...	100	56	3	30.5	5.5	5	0	0	......	Never lived in country.

Thirty-one cases of uncinariasis out of 57 = 54 per cent.
Average eosinophilia for positive cases, 6.85 per cent.
Average eosinophilia for negative cases, 2.50 per cent.
Average weight of positive cases, 141 lbs.
Average weight of negative cases, 148 lbs.
Average gain in weight after treatment, 0 lbs.

* N means negative history for ground-itch.
P. means positive for ground-itch.
Xlnt. means "Excellent."

TABLE II. FIFTY-SEVEN UNSELECTED SOUTHERN BRED SOLDIERS IN THEIR FIRST ENLISTMENT PERIOD (THREE YEARS)*

Case No.	Age.	Years in Army.	Height, inches.	Weight before treatment.	Weight after treatment.	Occupation at time of enlistment.	Occupation previous to enlistment.	Birthplace.	Residence.	History of ground itch.	Years since ground itch.	Color.	% hemoglobin.	% polynuclears.	% eosinophiles.	% lymphocytes, small.	% lymphocytes, large.	% transitionals.	% mast cells.	Number of ova found in stool.	Number of worms found after treatment.	Remarks.
44	34	¼	64	140	....	Mechanic	Cook	Ga...	Ga...	N	....	Good...	90	76	3.5	16	3	1.5	0	0	......	Never lived in country.
45	23	1	68	143	146	Fireman	Fireman	Miss.	Miss.	N	....	Good...	90	56	4	31	7	2	0	Many..	2	Never lived in country.
46	22	1	68	151	....	Student	Farmer	Miss.	Miss.	P	10	Good...	90	68	3	20	5	3	1	0	......	
47	21	1	67	126	135	Farmer	R. R. Laborer	Miss.	Miss.	P	7	Pale...	80	63	7.5	24	2.5	3	0	Very many	82	
48	23	1	69	166	167	Fireman	Farmer	Miss.	Miss.	P	10	Pale...	100	64	6	23	4	3	0	Many..	35	
49	22	½	72	146	....	Machinist	Machinist	Miss.	Va...	N	....	Good...	100	60	2	28	3	7	0	0	......	
50	29	¾	70	146	....	Engineer	Farmer	Ala..	Miss.	P	?	Good...	90	53.5	7.5	29.5	4	5.5	0	Very few	2	
51	19	1	65	145	138	Farmer	Farmer	Ala..	Miss.	P	8	Good...	90	42.5	8	37	7.5	4	1	Many..	35	
52	22	¾	66	115	124	Farmer	Farmer	Ala..	Miss.	N	....	Good...	90	46	12	32.5	6.5	2.5	0.5	Very many	13	
53	26	1¼	69	140	140	Laborer	Farmer	Ala..	Miss.	P	12	Good...	100	58	4	36	1	1	0	Very few	3	
54	20	¾	68	144	132	Smith	Smith	Miss.	Miss.	N	....	Good...	100	62.5	4.5	26.5	2.5	3.5	0.5	Few....	4	
55	14	½	67	135	....	Farmer	Factory	Miss.	Miss.	P	2	Fair....	100	66	3.5	24	4	2	0.5	0	......	
56	25	1	70	149	....	Stock Farm	Same	Miss.	Miss.	N	....	Xlnt....	100	58	2	32	6	2	0	0	......	
57	19	1	65	143	149	Canning	Canning	Tex..	La...	N	....	Good..	90	60	7	24	4	5	0	Few....	0	Never lived on farm.
58	23	1	70	138	142	Fireman	Farmer	La...	Miss.	P	2	Good...	90	66.5	2.5	25.5	2.5	3	0	Few....	55	
59	28	1	65	123	....	Boxmill	Painter	La...	La...	N	....	Fair...	90	36.5	0.5	49	5.5	8.5	0	0	......	Never lived in country.
60	25	1	70	135	135	Sawmill	Farmer	Miss.	Miss.	P	18	Good...	90	30	6	32	15	17	0	Few....	13	
61	19	1	69	134	....	Section man	Section man	Miss.	Miss.	P	6	Good...	100	47	1.5	37	5.5	8.5	0.5	0	......	
62	31	1	65	115	116	Lumbering	Farmer	Miss.	Miss.	P	18	Good...	100	63	8	24	3	2	0	Many..	31	
63	23	1	69	136	139	Pile driving	Farmer	Fla..	La...	N	....	Good...	90	65	5	24.5	1.5	4	0	Few....	11	
64	30	1	70	160	....	Photographer.	Farmer	Tenn	Tex..	N	....	Good...	100	55	1	29	8	7	0	0	......	
65	29	1¼	65	138	139	Machinist	Farmer	Fla..	Fla..	P	4	Pale...	90	41	5	48	2	4	0	Few....	32	
66	22	1	69	132	132	Express	Express	Tex..	Tex..	N	....	Fair...	90	54	6	32.5	3	3	1.5	Very few	1	Never lived in country.
67	19	1	67	139	....	Engineer	Clerk	Ga...	Ala..	P	12	Fair...	90	58	2	33	4	3	0	0	......	Never lived in country
68	23	1	66	146	140	Clerk	Farmer	Ala..	Ala..	N	....	Good..	90	55	5	26	5	7	2	Few....	18	
69	23	½	69	130	127	Farmer	Farmer	La...	La...	N	....	Good...	90	59	13	23	2	2	1	Few....	10	
70	22	1¼	70	151	148	Logging	Farmer	Miss.	Miss.	P	3	Good...	90	49	11.5	28	6	5	0.5	Few....	1	
71	23	½	65	142	....	Log scaler	Log scaler	Miss.	Miss.	P	6	Fair...	80	59	2.5	30	3	5	0.5	0	......	
72	26	¾	70	164	176	Laborer	Farmer	Ga...	Ga...	N	....	Good...	100	62	5	23	5.5	4.5	0	Very few	13	
73	21	½	68	151	146	Coal miner	Lived on farm	Ala..	Ala..	N	....	Good...	100	52	8	37	3	0	0	Many..	27	
74	24	½	69	189	....	Salesman	Clerk	La...	La...	N	....	Good...	100	59	0	31	4	5	1	0	......	Never lived in country,
75	19	1	67	132	136	Laborer	Laborer	Miss.	Miss	P	5	Pale...	100	83	6	9	1	1	0	Very many	77	Laborer in city. Never lived in country.
76	24	1	67	153	....	Carpenter	Farmer	Miss.	Miss.	N	....	Fair...	90	51	6	32.5	4	6	0.5	0	......	
77	28	2	67	138	....	Bricklayer	Express	La...	Ala..	N	....	Xlnt...	100	53	7	26	5	6	3	0	......	Never lived in country.
78	21	1½	70	160	164	Cotton mill	Farmer	Ala..	Fla..	P	7	Fair...	100	62	4	26	6	2	0	Few....	75	
79	22	¾	69	137	138	Fireman	Scholar	Miss.	Miss.	P	12	Good...	100	53	4.5	33	4.5	5	0	Very many	99	
80	25	1½	65	124	....	Waiter	Clerk	Ga...	Ga...	N	....	Pale...	90	57	2	20	12	8	1	0	......	Never lived in country.—Syphilitic.
81	25	2	68	159	144	Lumbering	Farmer	Ala..	Ala..	P	15	Good...	100	54	1	27.5	10	7.5	0	Very few	1	
82	23	2	68	165	165	Lumbering	Farmer	Ala..	Ala..	P	11	Good..	90	48	11	31	4.5	3.5	2	Very few	3	
83	23	2	68	132	137	Electrician	Electrician	Ala..	Ala..	N	....	Fair...	90	24.5	13.5	51	5	5	1	Very many	38	
84	33	2	72	184	....	Lumberman	Farmer	Miss.	Mo...	N	....	Fair...	100	49.5	0.5	39	5	6	0	0	......	Lived in Mo. last 13 years.
85	33	1	67	150	....	Farmer	Farmer	Tenn	Tex..	N	...	Good...	90	48.5	5	34	5.5	6.5	0.5	0	......	
86	23	1¼	64	123	117	Laborer	Laborer	Miss.	Miss.	N	....	Fair...	80	45.5	3.5	35	10.5	5.5	0	Very few	5	
87	28	2¼	74	175	173	Farmer	Farmer	Miss.	Miss.	P	10	Good...	100	35.5	7	42.5	9	5	1	Very few	15	
88	29	1½	66	139	....	Electrician	Merchant	La...	La...	N	....	Good...	90	65.5	0.5	16.5	9	8	0.5	0	......	Never lived in country.
89	26	1	67	142	....	Telegrapher	Clerk	Tex..	Tex..	N	....	Good...	100	68	6	21	3	1	1	0	......	
90	22	2¼	69	161	....	Telegrapher	Telegrapher	Tenn	La...	N	....	Pale...	90	61.5	1.5	21	6.5	9	0.5	0	......	
91	24	2	67	138	....	Carpenter	Carpenter	Miss.	Miss.	N	....	Pale...	90	64.5	4.5	26	2.5	2.5	0	0	......	Lived on farm till 16 years old. Never farmed.
92	23	1½	72	163	....	Drummer	Fireman	La...	La...	N	....	Fair...	90	54	4	37.5	3	1	0.5	0	......	Never lived in country since 8 years old.
93	24	1½	68	137	139	Millman	Farmer	Miss.	Miss.	P	10	Good...	100	38	12	47	1	1	1	Very many	24	
94	31	1	72	184	....	Farmer	Farmer	Miss.	Miss.	N	....	Xlnt...	100	45	3.5	36.5	11	3.5	1.5	0	......	
95	27	2	69	149	....	Clerk	Clerk	Ala.	Tenn	N	....	Good...	90	74	0	23	1	1	1	0	......	Never lived in country.
96	23	¾	65	138	136	Brakeman	Millhand	N. C.	S. C.	P	15	Good...	100	62.5	3	24.5	4	6	0	Few....	10	
97	22	1¼	66	140	136	Circusman	Farmer	Tex..	La...	N	....	Pale...	80	56	12.5	28	1.5	1	1	Few....	0	
98	32	¾	69	145	....	Machinist	Ironworker	Va...	Va...	N	....	Fair...	90	61.5	5	27.5	2.5	3.5	0	0	......	Few ova tricocephalus dispar.
99	23	1¼	65	136	....	Salesman,	Salesman	Ky...	La...	N	....	Good...	100	57	2	35.5	3.5	2	0	0	......	Never lived in country.
100	24	1½	70	144	....	Smith	Painter	Va...	Ala..	N	....	Good...	100	56	3	30.5	5.5	5	0	0	......	Never lived in country.

Thirty-one cases of uncinariasis out of 57 = 54 per cent.
Average eosinophilia for positive cases, 6.85 per cent.
Average eosinophilia for negative cases, 2.50 per cent.
Average weight of positive cases, 141 lbs.
Average weight of negative cases, 148 lbs.
Average gain in weight after treatment, 0 lbs.

* N means negative history for ground-itch.
P. means positive for ground-itch.
Xlnt. means "Excellent."

non-infected cases 2.2 per cent. In the 83 negative cases, only 9 subjects showed an eosinophile count over 5 per cent., and, of these, 2 were infected with *Trichocephalus dispar,* which doubtless caused the eosinophilia. From these observations it appears that an eosinophilia of over 5 per cent. is a very strong point in favor of infection with an intestinal parasite, but that one below 5 per cent. is of no value in excluding infection with *Necator americanus.*

THE PARASITES

Of the 64 patients in whom ova of uncinaria were demonstrated in the feces, 4 left before treatment. The remaining 60 patients were treated in the usual manner with 4 gm. of thymol, and worms were recovered from the stools of 56. The smallest number found was 1, the largest 99, and the average number per patient was 16. Whether this represents the entire amount of infection is not yet known, as very few of the patients have been re-examined since treatment, and it is probable that some worms still remain in many of the patients. The majority of the men interrogated some weeks after treatment reported that they felt better than before; one did not feel so well, and a few noted no change, these last being patients from whom only 2 or 3 worms were obtained.

All of the parasites are believed to have been American hookworms. Specimens from half of the cases were sent to Dr. C. W. Stiles for identification, and he reports that all were *Necator americanus.*

In the examination of the entire 147 men, it was surprising to find the ova of other parasites in only 3 cases, all of the 3 being infections with *Trichocephalus dispar.*

LONGEVITY OF THE HOOKWORM IN THE INTESTINES

The length of time the parasite will live in the intestines seems to be in doubt, but that it may sometimes be a period of several years appears probable from my findings. The habits of the soldier and the sanitary conditions at this and practically all other army posts are such that reinfection with uncinaria larvæ is not probable. In the new recruits examined, 67 per cent. of infection was found; in the soldiers in their first enlistment, 54 per cent., and in those in subsequent enlistments, 11 per cent. This apparently indicates that there is a tendency for the worms in the soldier's intestine to die out gradually. This tendency, however, is not always rapid, as is shown by the persistence of the infection in some cases even to the fourth, sixth and seventh years of service.

DIAGNOSIS

In the cases like those covered by this report the general appearances and ordinary physical examination are of no diagnostic value. Diagnosis must rest solely on the microscopic findings. As stated above, an eosinophilia of over 5 per cent. is very suggestive, but one below that by no means excludes uncinariasis. In these light infections the finding of ova in the feces is often a tedious process. I made my examinations by mixing a bit of feces with water and covering with a seven-eighth-inch cover-glass. In Tables 1, 2 and 3 I have recorded the number of eggs in the stools as "very few," "few," "many" and "very many." If two or more slides were gone over before a single egg was found, the record "very few" was made. If one or two ova were found in a slide, the record was "few." The tables show "very few" in 18, or 28 per cent., of the 64 cases, which means that at least two slides were gone over before an ovum was found. In several cases six or eight slides were examined before the first egg was discovered.

In some cases the number of eggs found in the feces seemed to bear no relation to the number of worms passed after the first course of treatment.

SOURCE OF INFECTION

In this series of cases, the findings coincide with previous experience as to the importance of rural life as a predisposing cause of infection. Among the 64 infected subjects, 53 gave a history of having at some time worked on a southern farm. Of the 11 remaining subjects 3 were laborers, 2 firemen and 1, each, a plumber, country blacksmith, expressman, brakeman, electrician and canning factory employé. Only 4 infected subjects reported never having lived in the country, and, of these, 1 was a laborer, 1 an expressman, 1 a locomotive engineer and 1 worked in a factory canning shrimps and oysters.

Among the 100 recruits and soldiers in their first enlistment, 74 had been farmers at some period of their lives, the percentage of uncinariasis among these being 81 per cent. This closely approximates the findings of some physicians who have asserted that in parts of the south 90 per cent. of the rural population is affected with hookworm disease.

Most of the men gave a history of having gone barefooted in childhood, and a little over half reported having had ground itch, but in most cases the last attack was stated to have been a great many years before, so it is doubtful if much importance can be attached to that feature in this series (Tables 1, 2 and 3).

RELATION OF UNCINARIASIS TO THE PHYSICAL DEVELOPMENT OF RECRUITS

It is considered by many recruiting officers that the physical development of the southern applicants for enlistment is below that of northern men, and it is known that a great number of southern men are rejected at the recruiting stations for poor physical development and weight under that required. The observations made by myself, as well as by other army surgeons, have given the impression that the southern recruits are poorly developed and poorly nourished. Some statistics from the records of the examination of recruits at Jackson Barracks confirm these impressions, as indicated by Table 4.

TABLE IV—HEIGHT AND WEIGHT OF RECRUITS

	Average Height.	Average Weight.	Relation of Weight to the Army Standard
149 recruits not born in south.........	66	145	13 lbs. above.
308 recruits born in the south	68 2/5	141⅔	2 1/3 lbs. below.
70 southern-born farmer recruits......	68 1/6	140	2 1/6 lbs below.
64 soldiers with uncinariasis.........	68 3/7	140½	3½ lbs. below.

Siler considers it probable that the poor development of the southern recruit is due to uncinariasis. In this connection these words of Stiles are of interest: "If infection occurs before puberty, it is likely to retard development, both mental and physical." My own work shows that the average weight of the infected cases was lower than that of the non-infected southern soldiers, though the difference is not very marked among the new recruits.

TABLE V—WEIGHT OF INFECTED AND NON-INFECTED SOUTHERN RECRUITS

	Average Weight.	Difference.
14 southern recruits not infected............................	143	
29 southern recruits infected................................	140¼	2¾ lbs.
26 southern soldiers in first enlistment non-infected...........	148½	
30 southern soldiers in first enlistment infected................	142	6½ lbs.

As seen in Table 4, the average weight of 64 infected soldiers, as compared with their height, was 3⅝ pounds below the army standard, while the average for 149 northern-born recruits was 13 pounds above.

Whether the eradication of the parasites at the age of the average soldier will lead to an increase in weight is left in uncertainty by my observations. Siler reports a constant gain in weight in recruits after treatment. My 29 recruit patients, weighed about five weeks after treatment, showed an average gain of 3½ pounds. It is not fair, however, to attribute a gain of weight in recruits solely to the fact that they have been relieved of their hookworms, because it has been found that under ordinary circumstances recruits gain weight as a result of the regular life, good food, excellent sanitary conditions and graduated exercises associated with the military life.

Among 34 seasoned soldiers, weighed on the average about one month after treatment, there was a total loss of 11 pounds, or about one-third of a pound per man. Some men gained markedly, while others lost as heavily. It is thought that further treatment of such as may be found still to harbor worms may show, if the patients be weighed one or two months later, after the effects of treatment have fully passed off, that eradication of the worms has favorably affected the weight.

PROPHYLAXIS

It is probable that any applicant for enlistment in the army who has a marked infection with uncinaria will be detected by the ordinary examination given a recruit. The light infections which escape the examining officer apparently do not affect materially the efficiency of the soldier and do not, in the patients' interest, urgently demand treatment. From the standpoint of prophylaxis, however, thorough treatment of the mild infections is of great importance both in the army and in civil life. It is probable that there are hundreds, perhaps thousands, of cases of mild uncinariasis in the army, some of which may be setting up new foci of infection in localities hitherto free from the disease. Just as the typhoid bacillus-carrier is a menace to the community, so is the hookworm-carrier, and the treatment of the comparatively few carriers in the military service and the countless ones outside the army will be one of the steps absolutely necessary if the disease in its severer manifestations is to be eradicated from the south.

CONCLUSIONS

1. Infection with uncinaria is very common among southern-bred soldiers during the first three years of service. In 100 men examined, 60 per cent. showed uncinariasis. Among new recruits the percentage of infections is at times as high as 85.

2. Southern-bred soldiers with more than three years' service show a much lower percentage of infection, only 11 per cent. in 33 cases.

3. The worms gradually die out, most of them during the first three years, and under the favorable sanitary conditions obtaining in the army at home reinfection occurs rarely, if at all.

4. The symptoms produced by a light infection with hookworms are so slight that they can not be detected by the usual methods employed by the examining surgeon, and diagnosis must be made with the microscope.

5. An eosinophile count of over 5 per cent. is very strong evidence of infection with an intestinal parasite, but one below 5 per cent. is no evidence against uncinariasis.

6. The parasite in probably all cases is *Necator americanus.*

7. In some cases the worm probably lives several years in the intestines.

8. In many light infections, the ova are difficult to find, requiring the complete examination of five or six cover-glass preparations.

9. Farm life is very important as a predisposing cause. Among 74 men who had farmed at some time, 81 per cent. were infected.

10. Most of the men had gone barefooted in childhood, and over half reported having had ground itch, though usually not since childhood.

11. Southern recruits are less well developed physically than northern ones.

12. Uncinariasis in childhood is a very probable cause of this underdevelopment.

13. Light infections do not materially affect the efficiency of the soldier, though the majority report that they feel more vigorous after treatment.

14. Treatment of the light infections is of great importance in any attempt to stamp out the disease.

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American Medical Association, One Hundred and Three Dearborn Avenue
CHICAGO

MILD UNCINARIA INFECTIONS

C. C. BASS, M.D.
NEW ORLEANS

Hookworm disease exists in a very large area of the civilized world, varying greatly in the extent of the infection in different localities. The Porto Rico Anemia Commission estimates that 90 per cent. of the population of Porto Rico are infected and that 30 per cent. of the deaths are due directly to this disease. No estimate can be placed on the number resulting from it indirectly. C. W. Stiles, who has especially directed attention to this disease in the southern states, has collected reports of many thousand cases all over the south. He is convinced that the death rate due directly thereto is very high, while that due indirectly to this disease is enormous. It is unnecessary to mention the importance of the economic side of the subject. The intensity of the infection varies greatly in different individuals.

It is intended to discuss in this paper briefly mild uncinaria infections (1) from the hygienic standpoint, (2) from the clinical side, and (3) to refer somewhat at length to certain manipulations in technic by which these cases can be more certainly recognized than by the ordinary examination of the feces.

HYGIENIC CONSIDERATIONS

For every well-marked case of uncinariasis in the infected section of the southern states there are several patients having from one parasite up to a number sufficient to cause the ordinarily recognized symptoms. The proportion of mild to severe cases varies with the extent of the infection in a given locality, but it is perfectly consistent that there should be very few medium to severe cases in a given locality while yet a large percentage of the entire population may be infected to some extent. This is particularly likely to be true where there are many negroes. Negroes do not, as a rule, show marked symptoms, even when infected with many parasites. Those who have many eggs in the feces usually show only slight or no anemia if the blood is examined.

Many of the mild cases are those of persons who wear shoes and in whom there is no history or little probability of skin infection. Adults are likely to fall in this class. This argues the probability of mouth infection in this class of cases.

Mildly infected cases should be treated and warned against soil pollution, just as severer ones, for they may be a source of infection to others and give rise to severe cases. Just here the southern negro demands special consideration. His habits and bad hygiene include soil pollution, which, as shown by Stiles and others, is the great source of hookworm disease. The infected negro is a source of infection to others, while he himself enjoys considerable immunity from the effects of the parasite. He here plays the same rôle as he does in the spread of yellow fever, which he has in a mild and usually unrecognized form. His immunity from the effects of yellow-fever infection is illustrated by the experience at Tallulah, La., in 1905. The number of cases was: whites 80, with 18 deaths; colored about 950, deaths 5. Though there may not be the same difference in susceptibility to the effects of uncinaria infection, I am sure it is very considerable. Mildly infected patients and infected negroes compare well with the typhoid or diphtheria bacillus-carriers or the chronic malaria patients.

CLINICAL CONSIDERATIONS

The symptoms of uncinariasis are not always in proportion to the number of worms present. This no doubt is influenced largely by individual susceptibility and individual capacity of blood regeneration. It frequently happens that a patient with many worms has few or no symptoms, whereas another patient with few worms may have severe anemia or other symptoms. I am convinced, however, that those who have mild infections generally do not have recognizable symptoms.

Out of 152 cases of infection seen in which the symptoms were not sufficiently marked to attract special attention—cases which were, therefore, properly classed as mild—in only 26 per cent. was there more than 4 per cent. of eosinophiles, and in only 6 per cent. of the cases was there more than 6 per cent. of eosinophiles. Complete blood examination was made in 62 of these cases. The average percentage of hemoglobin was 90. The average number of red corpuscles was 5,125,000.

Of the 152 cases, 32 per cent. gave a history of more or less indigestion; 34 per cent. gave a history of pains and tenderness on pressure in the right side of the abdomen.

It is through the courtesy of Dr. J. B. Elliott, Sr., former professor of medicine in Tulane University, who was one of the first in our section to recognize the rôle of uncinariasis in producing a variety of vague digestive and abdominal symptoms, that I have seen several of these cases. The following cases are illustrative:

Case 1.—J. B., aged 39, male, white, merchant, was well developed and looked fairly well; had never had ground itch; lived in town. He had had vague pains in the right side of abdomen as long as he could remember; said he was nervous and had "indigestion." Pains were not related to the time of eating. Physical examination failed to reveal anything abnormal. There were a few eggs in the stools; fourteen worms were recovered. The patient recovered entirely and gained nine pounds in nine weeks.

Case 2.—L., aged 61, white, farmer's wife, had had no ground itch. The negroes on the plantation had it. The patient had had pains in the right side and uneasiness in the abdomen for the past six years, not related to meals; tenderness was not present. Physical examination showed nothing abnormal. There were a few eggs in the stools; no anemia. The patient recovered on treatment with thymol. Eight months later she was still well.

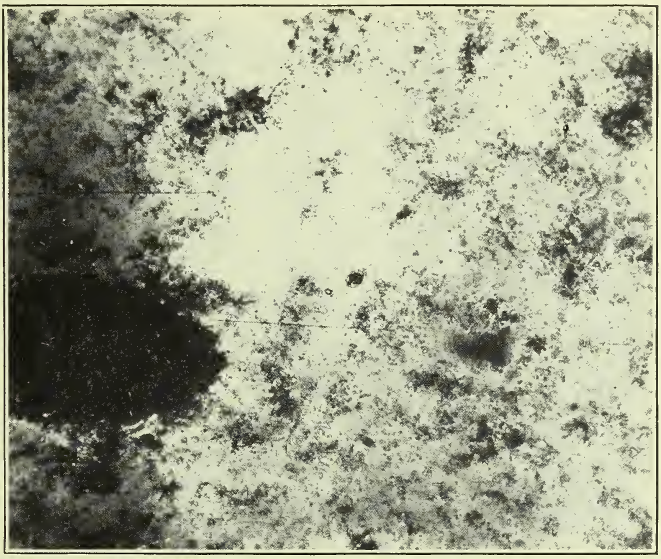

Fig. 1.—Photomicrographic view of feces containing uncinaria eggs. Only one egg is shown.

Case 3.—Paul H., aged 42, male, white, lawyer, complained of indigestion and frequent headaches. He had tenderness in the right side of the abdomen. There were a few eggs in the stools. The patient was relieved of indigestion and headaches after the first course of thymol.

It would be impracticable to relate here enough cases to prove that the vague and indefinite symptoms referred to are frequently due to hookworms and that their occurrence in uncinariasis is not a coincidence. One who has met a large number of such cases and seen the prompt relief following treatment becomes convinced, I believe, that a very few worms may give rise to such symptoms without the production of anemia.

All who have had much experience with the disease have, however, seen cases with few worms and severe anemia. Hypersusceptibility to the toxin or possibly anaphylaxis may explain this. These cases form a striking contrast to what is seen in the negro with his many worms and no symptoms. Such instances should be regarded as cases of uncinariasis of medium or marked severity. They are often unrecognized through insufficient examination of feces. Many of the patients have had severer infection which has been reduced, but they have been unable to recover from the effects of the toxin. It is possible that old parasites may cease to ovulate long before they die. This hypothesis would explain cases in which there are few eggs and severe symptoms.

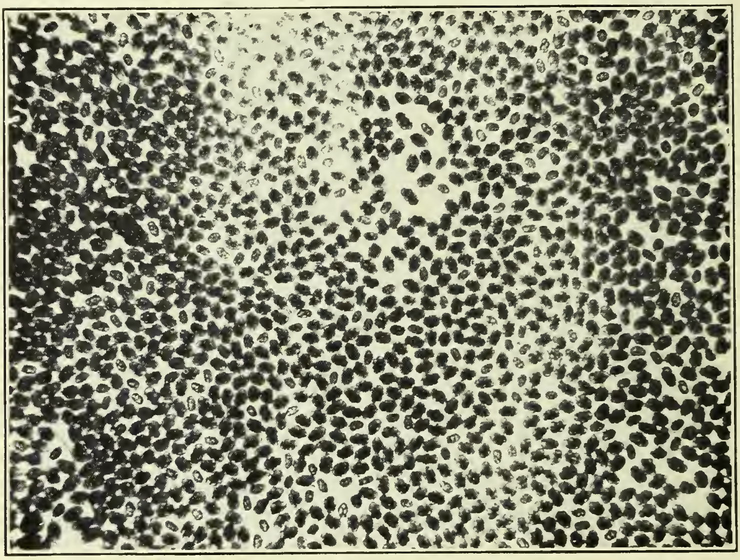

Fig. 2.—Eggs, practically free from fecal matter, obtained from specimen shown in Figure 1.

RECOGNITION OF THE OVA

The recognition of infections in which there are only a few parasites, or the determination of the moment when all parasites have disappeared under treatment, is not always easy. When many eggs are present, a positive report is easy to make; but when very few eggs are present it may require a long search over many slides before any can be found. To make a conscientious and reliable negative report, one must look over many slides if the ordinary technic is followed. I want to call attention to certain modifications of technic which make the examination far more reliable and save much time and labor. Following this technic one should find eggs if only one laying worm is present. This method of procedure is based on recognition of the specific gravity and shape of the eggs in relation to that of other material of the feces. Feces consist largely of bacteria, undigested food particles and crystals, insoluble grit, etc. The specific gravity of these different elements varies considerably. The specific gravity of fresh uncinaria eggs is between 1050 and 1100. When they grow old this is increased in many specimens.

A quantity of feces is well diluted with water, one in ten, and strained through gauze to get rid of coarse particles. This is centrifugalized, the fluid poured off, the centrifuge tube refilled and centrifugalized again until all the diluted feces have been used. The precipitate is rewashed several times with water as long as anything can be washed out. To know just how long to continue the centrifugalization is the secret of success. One must learn just what is the proper time for his centrifuge. It should be carried out at high speed and just long enough to throw the eggs to the bottom. Too long centrifugalization defeats the purpose. With a centrifuge running 3,500 revolutions per minute, ten seconds at first, when there is much matter, and then four to five seconds is usually

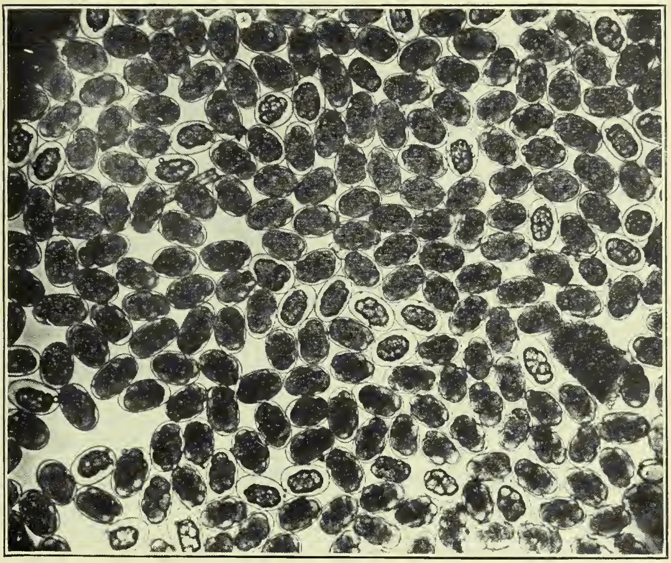

Fig. 3.—Higher-power view of eggs shown in Figure 2.

the proper time. The centrifuge must be steady. This gets rid of most very small things, those having flat rough surfaces and those having a specific gravity about that of water. Now the precipitate should be washed as before, using calcium chlorid solution of a specific gravity up to 1050. (Calcium chlorid is preferable to other salts because of its hygroscopic property. This was suggested by Professor A. L. Metz.) This disposes of everything having a specific gravity below 1050, and the precipitate may now be examined. There frequently remains a considerable amount of material, much of which is considerably heavier than the eggs and of such a character that it interferes much with their recognition. This material may be removed by centrifugalizing with a solution sufficiently heavier than the eggs. A solution with a specific gravity of 1250 is very satisfactory. In such a solution the eggs go to the top and other material below. With an appropriate pipette one may remove a few drops from the surface and examine, or, what is still better, pour off some of the top fluid containing eggs, dilute with water sufficiently to bring the specific gravity below 1050 and centrifuge again. The precipitate will now contain most of the eggs contained in the original amount of feces and may all be put on one slide and examined. One such slide contains as many eggs as could be found in several hundred ordinary slide preparations of feces.

With this technic I was able to recover 96 per cent. of 1,000 eggs put in one ounce of feces, 94 per cent. of 100 eggs in the same quantity, and 60 per cent. of 10 eggs in one ounce. From specimens containing many eggs they may be obtained practically free from anything else. The accompanying illustrations show the results obtainable. I am indebted to Professor Beyer for making the photomicrographs from which the cuts were made.

The procedure may be of service when it is desired to obtain quantities of eggs free from feces for experimental purposes. It should be used before making a negative report or pronouncing a patient under treatment to be positively free from parasites. Good results can be obtained only with fresh specimens, and preferably those taken following a dose of epsom salts. In old specimens the specific gravity of the eggs may go even above 1250.

Before making use of this technic on questionable specimens the investigator should familiarize himself with just what is accomplished by the different steps, using specimens containing many eggs. Unless he does this and also tests his centrifuge he will be disappointed. Solutions of calcium chlorid of several different strengths should be used when it is desired to get eggs absolutely free from other material, but for ordinary diagnostic work two solutions, one of a specific gravity of 1050 and one of 1250, are sufficient. Washing with water alone is of much service.

741 Carondelet Street.

Reprinted from The Archives of Internal Medicine,
June, 1909

AMERICAN MEDICAL ASSOCIATION, ONE HUNDRED AND THREE DEARBORN AVENUE.
CHICAGO

Reprinted from the New York Medical Journal for May 1, 1909.

Discussion.

Dr. W. S. THAYER, of Baltimore, said that it would be of great interest to try to study the stools for the ova of *Strongyloides stercoralis* by the method described by Dr. Bass, in order to determine the relative measurements of these eggs and those of uncinaria. The eggs of the former were very rarely found in the stools, and when they were found they were so like uncinaria eggs that there was sometimes a question as to their identity. Dr. Thayer doubted whether the eggs found in Dr. Bass's first case were those of strongyloides. The eggs obtained were those hatched outside of the body, which were not the same as those hatched in the intestine.

Dr. GEORGE DOCK, of New Orleans, said that he thought that a great deal more work should be done in detecting mild cases of uncinariasis with atypical symptoms, many of which could undoubtedly be remedied by treatment. He also thought that it would be interesting to find out how much of the aberrant psychic condition in certain sections of the country might be due to such infections.

Dr. JOHN M. SWAN, of Philadelphia, said that he had had an opportunity to study a patient who was a native of Alabama who had had several epileptoid convulsions. The patient was twenty-five years old and a traveling salesman. He had had epileptoid attacks of considerable severity at intervals of about a month. Examination of the blood showed an eosinophilia of 13.4 per cent. On examining the stools, a fairly large flagellate infection was seen.

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The patient was put on appropriate treatment, and within a short time the flagellates had disappeared, and the eosinophile count fell to 3.4 per cent. in a total leucocyte count of 18,000. The patient then improved very much in health. He had one other convulsive attack, which was of a true epileptoid character. After two months there was no recurrence of the convulsions, and just before the patient was to return to his home another blood study showed 22.0 per cent. of eosinophiles. In spite of repeated examinations of the fæces, Dr. Swan failed to discover uncinaria eggs; yet he felt reasonably sure that a proper technique might have discovered these eggs in the stools. He thought that the method suggested by Dr. Bass would have cleared up this point. In the only other case of uncinariasis that Dr. Swan had seen during the last three years the diagnosis was indicated by an eosinophilia of 8.4 per cent., and uncinaria ova were found in the stools in fairly large numbers by means of the ordinary technique.

Dr. JOSEPH F. SILER, of Fort Jay, N. Y., said that the question of prophylaxis of uncinariasis ought to be more thoroughly studied. He thought that the South would never be rid of the hook worm unless the question was taken up by the government. He believed that the society should try to have this work undertaken by the Federal authorities. The fact that practically all the children of the South were infected made him conclude that if that section could be rid of the hook worm, a great deal would be done for humanity. The cases were very widely scattered, and the disease practically riddled the whole of the southern country.

Dr. CHAMBERLAIN said that his cases were widely distributed. They came from every State in the South, as far north as Maryland. Consequently it appeared that the disease was universal throughout the southern States.

Dr. Bass said that the question of ridding the South of uncinaria infection was of very great economic importance. He thought, however, that the problem was one of education rather than of legislation, as it would be impossible to force the layman by law to observe such sanitary measures as would be necessary to prevent the disease. He must be educated to the necessity of avoiding such infection and in his relation to infection of others.

Dr. Bass said that he had not been able to apply the method to a large number of the parasitic eggs. He had used it for *Trichocephalus trichiuris* and the ordinary ascaris, though it did not apply well to ascaris eggs, because their coating was rough and they did not go down any faster than the other coarse material of the fæces. The albumin coating of the ascaris eggs also rapidly absorbed the salt solution, and they soon came to be of the same specific gravity as the salt solution.

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MALARIA:

With Special Reference to What is Not Malaria Fever*

JOHN PELHAM BATES, M.D.

LECTURER ON TROPICAL DISEASES, VANDERBILT UNIVERSITY, MEDICAL DEPARTMENT, NASHVILLE, TENNESSEE; FORMERLY PHYSICAN IN CHARGE, SECTION F, ANCON HOSPITAL.

I shall discuss in this paper only the quotidian form of malaria fever: "bilious remittent fever," "estivo-autumnal fever," or simply malaria fever. I shall attempt to show that in the study of this form of malaria we have studied not alone malarial infection, but have studied many other diseases along with it—complications which we have accepted as a part of its symptomatology—accepting these symptoms as variations from its specific course and reasoning from this false premise, we have been led widely astray.

And we have in this manner learned to be content with the term malaria to cover any number of obscure troubles, which may be attended by a quotidian or continuous fever, reasonably short in its course, and which has little or no physical signs or objective findings to account for it.

It is admitted at the outset that the failure to diagnose malaria per se is one of the remotest probabalities, but if we reverse the proposition, I can assert, without fear of contradiction, that the diagnosis of short irregular febrile attacks as malaria fever is one of the most common errors of diagnosis in medicine.

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*Read by proxy at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10, 1909.

It is my purpose to discuss this confusion in the diaignosis of this disease: how it has arisen; to show how it may be avoided; and to show also that malaria is the simplest of all diseases, as well as the most amenable to treatment.

Almost all diseases are said to have exceptions to the rule, that is, a certain train of symptoms are set down to them as being characteristic, and such variations from these characteristics as may appear are then described as the exceptions.

Malaria fever of all diseases is burdened with the greatest number of these exceptions, and with the widest variations. These exceptions are traditions, hoary with age, backed by eminent authority, universally accepted by the laity, and almost so by the profession.

Before the discovery of the malaria parasite, when the diagnosis depended on the clinical phenomena, the cold stage, the hot stage, and the sweating stage, errors in diagnosis, under these circumstances, were inevitable. We were certain then to include other diseases having the same phenomena under the diagnosis of malaria. Some of those old errors are still with us. And later, observers with no post-mortem facilities at hand for a final solution; with only the microscopical findings and clinical course to conclude from, have studied not only malaria, but a part of many other diseases along with it. These latter errors were too quite to be expected. We were looking for and expecting all kinds of variations, we had the dictum of the masters for them, why should we not find them? The pathologist even finds it difficult to free himself from the influence of these old beliefs. In cases of death from very acute illness the pathological findings are sometimes indefinite, and in malarial climates malaria pigment is often present in the bone marrow and spleen in such deaths as these. How easy to let this go as malaria and argue toxemia as the cause of death. All these things have been the contributing cause for our confusion in malaria; they have become a part of our faith, and in our minds a part of the disease.

TOXEMIA IN MALARIA.

If there is any toxemia at all given off during the cycle of the development of the malarial parasites, it must be extremely small and of minor significance. If this were not so, how could we have the amelioration of symptoms and feeling of comfort that comes to the patient in the remission of the fever. Celli's experiments, by injecting large quantities of blood serum from patients in paroxysm of malaria into other individuals, were entirely negative of results. Taking these two facts into consideration, the comfort of the patient in the remission of fever, and Celli's findings, it seems to me to clearly prove the minor significance of the toxemia.

PATHOLOGY.

Beside the engorgement of the spleen and liver, the pathology of malaria is principally in the blood. It is the simple destruction of the red blood cells by the maturing parasites, setting free hemaglobin, and the consequent lowering of the physiological function of these cells, in proportion to the number so destroyed. In addition there are the irritant products of pigment and the sporules. In pernicious cases, and in cases of impending death, the blood picture is a most striking one. The hemaglobin is reduced to fifty per cent or lower. The blood is drawn from the lobe of the ear with considerable difficulty, and when it exudes it is dark and grumous and clots quickly. Spread upon the slide, the leucocytes are seen to be enormously increased; the large, the small, and the polynuclears are crowded with pigment. The white cells will count from 20,000 to 40,000 or over. This increase of the whites is perhaps a relative one. The red cells are of every conceivable shape and size, and take the ordinary stain so deeply they are almost black. In addition to the parasites seen, nucleated reds are present in large numbers. Following this case to autopsy, in the smears from the cerebrum and cerebellum, we find in the capilaries and venus radicals that the blood cells are almost totally replaced by full grown parasites and pigment, and such red cells as remain in the vessels contain parasites of all ages. It is reasonable to assume that the same condition is present in the entire capillary system.

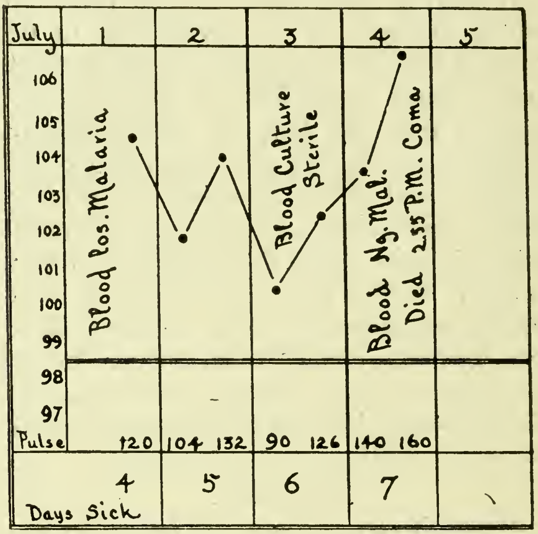

Chart 1.—Case J. G. Undertermined infection. Pathological diagnosis.

Keeping in sight of the fact that there is little or no toxemia in the cycle of developments; that it is without organic lesions, and its principal pathology is a periodic and acute hemolysis; and that the cell elements destroyed are physiologically and constantly reproduced, explains the low mortality and the simplicity of this disease. Its amenability to treatment is due to the above hypothesis also. As soon as the parasitic cycle is checked, all symptoms disappear and the blood functions promptly return to normal. All workers in fresh blood specimens are familiar with the agressive phagocytic action of the white blood cells on the full grown malaria parasites. On account of this function the leukocytes must be the scavengers that finally clear the blood stream of the pigment and other products of cell destruction.

CONFUSION OF DIAGNOSIS.

Malaria is not by any means the only disease characterized by irregular fever, chills and sweats. Moreover, malarial infection may be present in a large number of other infections and so-called constitutional diseases. I append a list of diseases in which malarial infection has been observed as a complication:

Typhoid fever, yellow fever, measles, pulmonary tuberculosis, pleurisy-effusion (tubercular), pericaridtis (tubercular), amebic dysentery (mild), non-amebic dysentery (mild), sub-acute articular rheumatism, acute and chronic nephritis, elephantiasis, kalar azar,[1] tonsilitis (mild), undetermined infection, relapsing fever.[2]

In view of the above facts, in the study of malaria, we must bear in mind that the finding of malarial parasites does not at all complete the diagnosis, but just begins it; that in studying malaria from the blood findings, and a few physical observations, we may be and often are studying malaria plus a number of other diseases. Therefore, to get a clear insight to the symptoms of malaria we must first be sure we have eliminated all intercurrent affections.

Fortunately, most of this long list of diseases, having malaria parasites along with them, have symptoms and findings so obvious that they offer very little difficulty in the final diagnosis. There are, however, several of them that require some mention in detail.

SOME OF THE DISEASES WE CONFUSE WITH, AND DIAGNOSE AS MALARIA.

We are continually diagnosing and studying the indefiinte fevers under the head of malaria. Such as the hyperprexias of the tropics. typhoid fever of moderate severity and especially the very mild cases. Incipient tuberculosis, and occasionally deep-seated suppurations and mild sepsis, and above all, old underlying diseases that in the course of an acute malaria, are roused to acute activity. I shall now take these up in detail.

HYPERPYREXIAS.

Most of these hyperpyrevias are fairly well differentiated from malaria, under various names, such as thermic fever, heat stroke, and so on. There are, however, hyperpyrexias, apparently specific in their clinical course, in which a considerable percentage have malarial infection. On admission of these cases to the wards little out of the ordinary will be noted, when suddenly the temperature will take an upward shoot to 106 or 107 Farh. The patient becomes wildly delirious for a short time, then turning to coma, in a few hours ends, in death. Or again, in some of these the temperature is high from admission and maintains a high level; delirium is constant, and wildly maniacal, necessitating forceful restraint in the bed. After three or four days the delirium subsides to a low muttering one, finally ending in

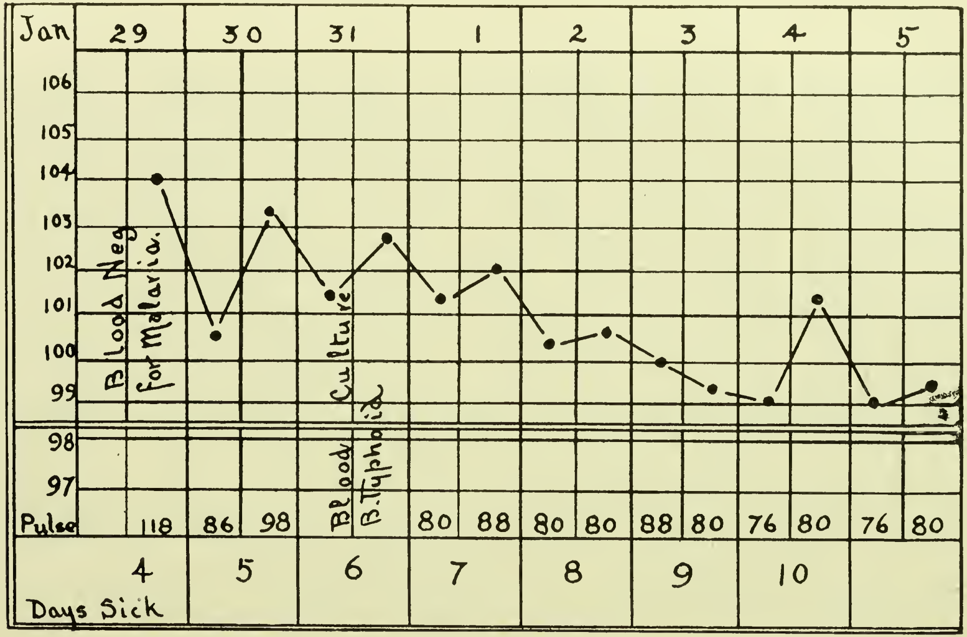

Chart 2.—Case J. W. Typhoid Fever. Note mal. like fever curve. Typhoid Fever positive by Blood Culture. Entire course of fever 10 days.

coma and death. In some of the cases enlargement of the liver and spleen has been noted.

I have seen ten or twelve deaths of these fevers, in one a very mild malarial infection was present on admission, and a few parasites were found at autopsy. The remainder of them, although some had parasites on admission, showed no evidence of malaria at autopsy, except pigmentation. To illustrate:

Case 1—J. G. ———, Chart 1, age 22, admitted July 1, 1908, died July 4, 1908. Ill three days before admission. Headache, fever, chills and vomiting. First illness in ten months. Physical examination negative. Urine, albumen, hyaline and granular casts. Blood examination, leucocytes 10,000, malaria parasites, infection moderate. July 3, blood culture, sterile. July 4, blood negative for malaria.

Complete pathological findings:[3] Infection undetermined origin. Acute spleenic tumor, lymphatic hyperplasia of intestine and spleen. Acute degenerative nephritis. Sub-pleural tubercle, right. Tuberculous lymphadenitis, right. No malaria parasites at autopsy.

Case 2.—H. C., age 18, admitted July 1, 1908, died July 5, 1908. Delirious on admission. No history obtained. Well nourished. Continuous, wild maniacal delirium, restrained in bed by force. Physical examination indefinite. Urine, albumen trace, hyaline and granular casts. Blood examinations: Leucocytes 8,600, negative for malaria. July 4, blood culture, sterile. Temperature on admission 105½ R. Maximum temperature 106½ R. Fahr. After a bath, July 5, p. m., there was a continued downward temperature until death, at 101½.

Complete pathological findings;[3] infection undetermined origin. Acute diffuse nephritis, sub-pleural, sub-pericardial, sub-mucous, ecchymoses of lungs, heart and pelves of the kidneys, respectively. Cloudy swelling of viscera. Acute spleenic tumor with increase of lymph tissue. Hyperplasia of lymph elements of ilium and colon. Icterus. Hematoma of ilium. Cultures, sterile.

It will be seen from these reports that these fevers are not malaria. From the mere fact that parasites were present in some of them, and death the ultimate end, with high temperature and coma, it does not follow that malarial infection must be the cause. I have had a large number of deaths from malaria—all of them verified at autopsy—and an excessively high temperature has not been a marked feature. Periodicity has been marked, and in spite of the fact that parasites of all ages were present in the blood. I have one chart of death from malaria, recording a temperature of 105½ Fahr., but most of my patients at death had only a moderate temperature or were sub-normal.

TYPHOID FEVER.

Here perhaps we have encountered the greatest stumbling block in differential diagnosis, and the hardest to get over. Malaria, I suppose, has never been mistaken for typhoid fever, not long at least; but typhoid fever, especially the mild form, is constantly called malaria. The reason for this confusion is that the mild form of typhoid fever is not unequivocally admitted to exist, and added to this, is the presence of malarial infection in from seven to eight per cent of all typhoid fever in malarial climates. In a recent work on typhoid fever,[4] by blood cultures, I have been able to show that the mild form does exist, and in the proportion of fully 30 per cent of all cases. In this mild typhoid fever, the febrile course lasts from eight days to two weeks, with striking quotidian features, and practically no marked symptoms (see

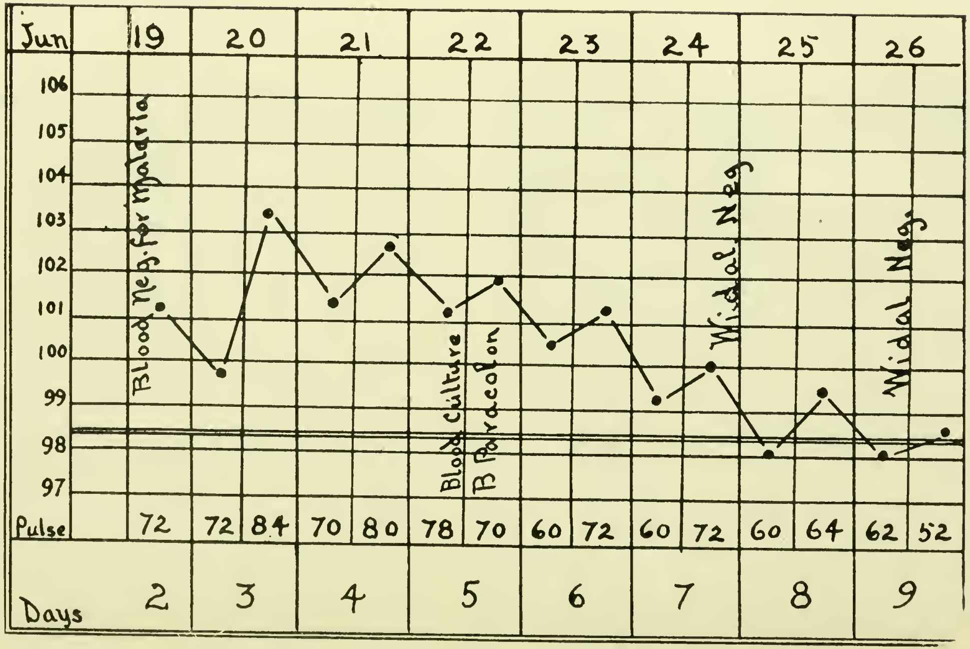

Chart 3. C. H. Typhoid Fever B. Paracolon. Note mal. like fever curve. Typhoid Fever positive by Blood Culture. Entire course of fever, 8 days.

charts Nos. 2 and 3). Then given a fever, indefinite in its symptoms, of short duration, with occasional malarial infection present, and a quotidian temperature, the natural conclusion would be atypical malaria, rather than atypical typhoid fever. Thus mild typhoid fever has been studied as malaria time out of mind, and is largely responsible for the belief that certain malarias respond only gradually to the treatment by quinine.

The symptoms that typhoid fever and malaria have in common are: occasionally the pointed tongue, nearly always enlarged spleen, and constantly quotidian and subquotidian temperature. Otherwise, they are widely different. In mild typhoid fever there is moderate headache, and it is usually frontal, or to one side. Some weakness is complained of, but no other pain. There remains a moderate desire for food, and the patient prefers to be up and around most of the day. In malaria, while it is true the height of the temperature is no criterion to the gravity of the infection, it remains the rule, that with a fever above 101 in acute malaria, we have a rather sick patient. He complains of severe headache, and pain in the neck near the junction of the cerebellum. Pain in the "small of the back," pain in the calves of legs, and weakness in the knees. More or less vomiting is present, and always a perfect willingness to get to bed during the paroxysm. Where these two infections are present in the same individual, quinine may at first reduce the temperature, or it may not. If it does reduce the temperature, it will rise again when the malaria subsides and typhoid infection gains the ascendency. In simple malaria quinine

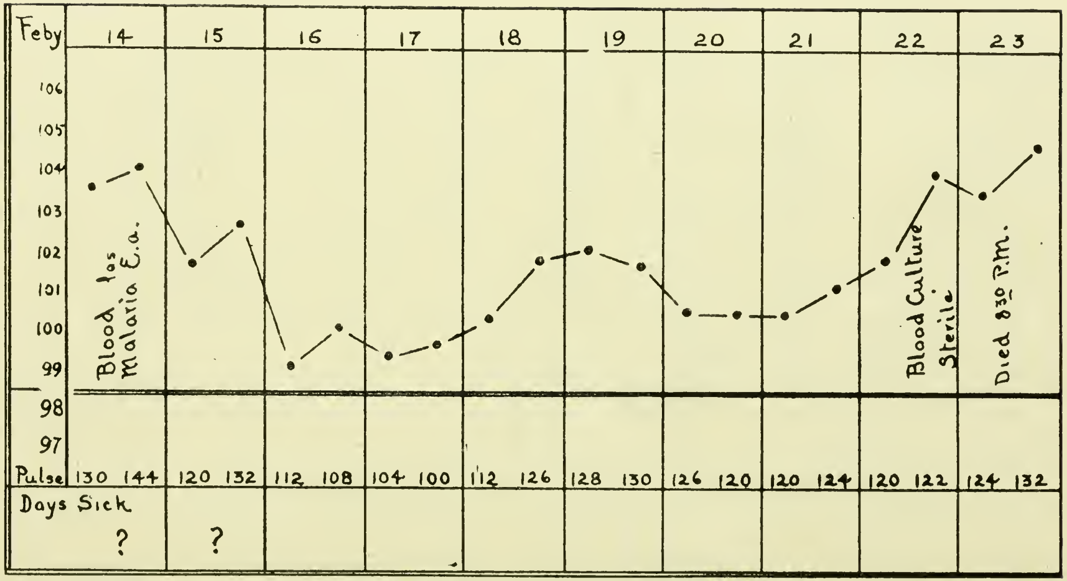

Chart 4.—C. G. Case. Malaria Fever Primary. Nephritis Secondary. Note second rise of fever as Nephritis Develops.

will always make a marked impression on the temperature in forty-eight hours.

INCIPIENT TUBERCULOSIS.

In incipient tuberculosis the temperature curve, the chilliness, the fever and the sweats, the short duration in the course of the recurrent attacks, with practically no physical findings, make the symptoms almost identical with malaria. Now comes the presence of malarial infection in tuberculosis to add to our confusion. I have no figures to show how large a percentage there may be of malarial infection along with tuberculosis. It is though large, and I have no doubt that all tuberculous patients who live in malarial climates have had, at some time or other, in the course of their illness, malaria, more or less severe. These patients never fail to come to us with the statement that they have had malaria a number of times. Some physician has diagnosed it malaria, or if not, he has supinely accepted the patient's own diagnosis. Thus you see how these cases have been studied as malaria, and often diagnosed as such.

To differentiate malaria and tuberculosis the most important point to appreciate is the fact that the two infections often occur in the same patient, and to never rest content with a diagnosis based upon the blood findings alone. Physical findings, together with the tuberculin tests, will now serve to clear the diagnosis.

LIVER ABSCESS AND DEEP-SEATED SUPPURATIONS.

Pain is not often a marked symptom in these conditions. Irregular and recurrent fever, rising to 100 or to 101 in the afternoon, with progressive loss of health, being the most marked feature. This is especially so in liver abscess. Most of these patients have had attacks of malaria, and usually come to the phy-

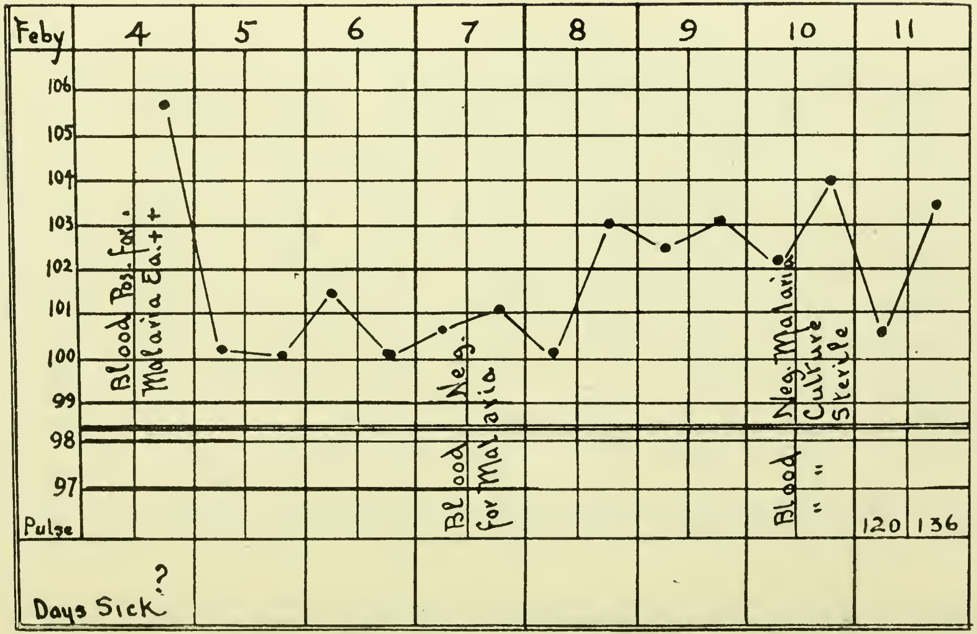

Chart 5.—Case J. W. Malaria Fever Primary. Nephritis Secondary. Note second rise of Fever as Nephritis develops.

sician for treatment, and not for diagnosis. His symptoms are vague, and he looks upon his case as chronic malaria, and expects you to do the same. You are likely to do so, especially if you hold to the old teaching or believe that certain malarias are resistant to quinine. With fever rising no higher than 101 or 102 as a maximum, quinine will control it in from thirty-six to forty-eight hours. If it does not do so, look upon this fever with suspicion. Blood examination will prove negative for malaria parasites. Leucocytosis will be noted, the count varying from 12,000 to 20,000 or over. A differential count will show the polynuclears to be eighty per cent or above. This will serve to point the direction of the diagnosis.

I wish to digress a little here to make some general statements on the effects of inflammatory leucocytosis on the malarial parasite. In the latter part of 1905 I first noticed in blood examinations, in cases of pneumonia, that after leucocytosis became marked, malarial parasites were always absent from the blood. Extending this observation over other inflammations, I found the same thing true in all of them. As I have previously remarked, all workers in fresh blood specimens are familiar with the aggressive phagocytic action of the white cells for the full grown malarial parasites. Therefore, on account of this phenomenon I can readily understand why, with an abnormal rise of the whites, say above 15,000, they soon clear the blood of the malarial invaders, and leave an open field for other pathogenic factors.

Then given a fever attended by leucocytosis and resisting quinine the idea of malaria should be no longer considered, and drenching with quinine should cease, and the real cause be sought for.

SO-CALLED CONSTITUTIONAL DISEASES.

We come now to a much more difficult class of diseases, a class that has certainly been charged as malaria, time and time again. And nothing short of the pathological diagnosis can convince the observer that he is dealing with anything other than malaria. These are cases where an initial attack of malaria has relighted some old underlying condition, or perhaps, has been the direct cause of a supervening malady; in either event, the fever continues long after malaria, properly treated, has ceased to be a factor.

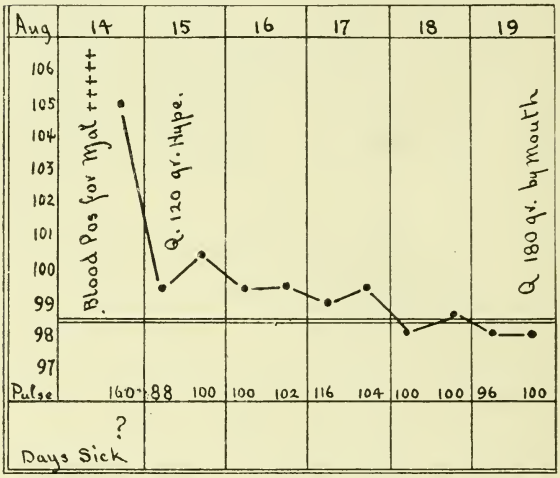

Chart 6.—Case D. B. Case 3. Malaria fever pernicious. Note malaria fever curve. No complications and on quinine.

To take up these general conditions in detail would lead us too far afield. They would include old organic maladies that are at times dormant and at times active, such as nephritis, gastro-intertinal inflammations, old recurrent dysenteries, chronic bronchitis and its tendency towards broncho-pneumonia. All of them may be aroused to acute activity by malarial infection, and they are often the direct cause of death. When any of the above troubles are relighted by malarial infection the picture in the beginning is one of frank malaria. Under treatment there is at first usually amelioration of symptoms, and generally a marked fall of temperature; at this stage a change for the worse takes place. It may be gradual, or it may be sudden. There may now be a long, and tedious illness, or end in death. To illustrate this I show charts Nos. 4 and 5. Both of these patients went to autopsy, and no malaria organisms were found, although quite a heavy infection was present on admission. Pathological diagnosis:[3] Nephritis and ilio-colitis, nephritis and broncho-pneumonia, respectively.

The lesson to be learned from these cases is when treating an initial attack of malaria, and quinine has been given in sufficient quantties to control the temperature or make a very decided impression upon it, and at this stage the fever begins to rise again, all treatment remaining the same, the second rise of fever is not due to malaria. If quinine will control in the beginning, it must follow that it will hold any exascerbation in check, so long as all conditions remain the same.

"CLINICAL MALARIA."

In a certain number of mild malarial infections, in others more severe where quinine has been given prior to examination, it is at times quite difficult to discover the parasite. The diagnosis is then based on the therapeutic test, and noted as "clinical malaria." Under this head the number of diseases that may be diagnosed as malaria depends on the variable ideas, and indifference—I ought to say "confident ignorance"—of the diagnostician.

The following table will show clearly the fallacy of this method of diagnosis. I take five hundred cases positive for parasites,[5] and five hundred cases with no parasites found.[6] The one thousand cases were of all classes and of all colors, and came into the hospital along together, getting quinine, 30 grains a day in solution, under exactly the same conditions, except the American patients.

CASES WITH FEVER.

No Parasites.		*Estivo-Autumnal Parasites-Positive.*	
8 days and over	7	8 days and over	0
7 to 8 days	15	7 to 8 days	7
5 to 6 days	63	5 to 6 days	33
3 to 4 days	200	3 to 4 days	214
1 to 2 days	215	1 to 2 days	233
CASES WITH NO FEVER.			
	0		13

This comparative table shows the fallacy of attempting a diagnosis on the symptom of quotidian fever, and moreover the wide latitude that will be taken by the diagnostician. The overplus in time of the "clinical" cases as compared with the cases with parasites are forty-five. Six of the seven positive cases, with fever seven to eight days, were complicated with several different diseases, such as "ascites," dysentery, uncinariasis, etc. And I must add that all the white Americans in these tables were taking their quinine usually twenty grains a day in capsules or tablets. And this, no doubt, has lengthened the total of days considerably. The results to be expected from quinine in capsules or tablets in a stomach upset by acute malaria as compared with quinine in solution needs no comment.

Four hundred and fifteen of these "clinical" cases were certainly malaria. The remainder may be anything.

This shows then that one blood examination, however carefully made, is not sufficient to pass as final in malaria blood work. It seems reasonable to me that in a moderate malarial infection there may be a time, after sporulation is complete and before the young forms re-enter the blood cells, when it would be quite impossible to discover anything. On this hypothesis then the patient's blood should be examined at three different periods in a day before declaring it negative.

I cannot accept the theory that malaria parasites can accumulate for a time in the blood of the viscera and be absent from the peripheral circulation; they live in the blood cells and the blood serum, and must move impartially and indifferently in obedience to the flow of this fluid; they cannot, therefore, be in any organ in larger numbers than another, except that the organ has a greater physiological supply of blood. For instance, the small spleen, with its enormous blood supply.

QUININE IN MALARIA.

Quinine is an absolute specific in malaria, and Manson[7] well says, "When you fail to cure by quinine a case of supposed malaria, it is not the drug that is at fault; it is the diagnosis. * * * Quinine, therefore, is not only of value in treatment, but also for diagnosis. Any fever which persists unmodified after forty-eight hours dosing with quinine, is not malaria fever."

Quinine should always be given in solution, hypodermically, or intravenously, with the patient at perfect rest, if death is impending or if the diagnosis depends upon the therapeutic test. Under these circumstances, quinine will completely control within five days any malaria fever amenable to treatment, and with no complications. Moreover, it will eliminate all parasites from all organs, if continued over a reasonable length of time, say two weeks, if patient is kept under proper control. I shall illustrate this by report of cases.

Case 3, Chart 6—D. B., admitted August 14, 1908. Unconscious, repeated convlusions, vomiting, hiccough almost continual. Physical examination: eyes staring and not jaundiced; tongue, broad and coated; all organs negative, except spleen, palpable. Blood examination; hemaglobin, fifty per cent. Malaria parasites positive, large numbers, and of all ages and crescents. Urine specific gravity 1015, granular casts, albumen trace. Treatment, quinine by hypo, 120 grains in twenty-four hours. Afterwards, quinine by mouth, forty-five grains daily. Recovery complete.

Case 4 —J. J., admitted July 9, 1908. Died July 16. First illness since arrival in country two month ago. Prior history indefinite. Sick five days before admission, with fever, headache and vomiting. Physical examination, old facial paralysis, right side, otherwise, negative, except spleen, palpable, arteries sclerotic. Mental condition, mildly irrational, sometimes getting out of bed, wandering aimlessly about the wards. Passing urine on the floor, or involuntarily in bed. Urine, specific gravity, 1028. Casts negative, albumen trace. July 12, sp. gr., 1030, hyalin and granular casts, albumen heavy. Blood July 9 positive for malaria parasites, large numbers, all ages, pigmented parasites and crescents. July 10, positive for large number of young forms, July 12, one parasite found on careful examination. Treatment, quinine, forty-five grains daily. Total amount taken, 335 grains.

Pathological diagnosis:[3] Acute degenerative nephritis. Pigmentation of spleen and bone marrow. No parasites.

Case 5, Chart 4.—C. G., admitted February 14, 1908. Died February 23. History indefinite. Time sick not known. Physical examination, negative. Vomiting more or less continuously, both medicine and nourishment. Blood examination, positive for malaria parasites, infection heavy. February 22, blood culture sterile; urine, albumen heavy, hyalin and granular casts. Treatment, quinine by hypo, February 14 and 15, 60 grains. February 16 to 23, by mouth, 45 grains daily. Total amount, 420 grains. Pathological diagnosis:[3] Acute nephritis and terminal bronchopneumonia. No parasites.

Case 6, Chart 5.—J. W., admitted February 4, 1908. Died February 11. History and physical examination, record lost. Blood examination; positive for malaria parasites. Infection heavy. February 2, negative for parasites. February 10, negative for parasites. Blood culture, February 10, sterile. February 11, blood negative for malaria. Treatment, quinine by mouth, 30 grains daily. Total amount, 250 grains. Pathological diagnosis: Nephritis and ilio-colitis. No parasites.

Case 7.—C. B., admitted July 12, 1908. Died July 22. Sick ten days before admission with headache, fever, vomiting and chills. Mental condition clear, extremely weak and occasional vomiting. Physical examination; bronchitis posterior; spleen, tender. Blood examination, positive for malaria parasites, all ages. Urine, sp. gr. 1020. Casts, negative; albumen, heavy. Treatment, quinine by mouth, 30 grains daily. Total amount, 320 grains. Pathological diagnosis:[3] Acute degenerative nephritis. Parasites in moderate numbers found at autopsy.

I could multiply the number of cases indefinitely, which had malarial infection on admission, and which died of intercurrent diseases or infections, to show the effect of quinine in the elimination of malaria parasites. Case 7, with parasites after ten days, on full doses of quinine, is a rare exception, however, the number found was so small that the malaria was not considered by the pathologist to be a causative factor of the death, but was simply noted, along with such other findings, as pigmentation, edema of the brain, etc.

As I have reported several acute nephrites after acute malarial infections, the question will arise, what part has malarial infection in the cause of nephritis? I do not know. It will be seen that the malarial infections reported here were probably primary. Most of the patients were from Barbadoes, and there is said to be no malaria there. I was trying to work out this question is why I happened to have this excess of nephritic cases to report. Different observers find in malarial cases evidence of kidney disturbance in from 47 to 58 per cent. In two hundred cases, tested by myself, I found evidence of nephritis in 42 per cent. Following this subject further, I analyzed the autopsy notes on forty deaths from malaria and hemaglobinuria, with reference to the kidney findings, with the following results: Acute cloudy swelling, 55 per cent; kidneys, normal, 25 per cent; acute degenerative, 15 per cent; chronic diffuse nephritis, 2:50 per cent; acute (one kidney) and chronic diffuse nephritis (one kidney) 2.50 per cent.

CONCLUSION.

Malaria is an extremely simple disease, and has no exceptions in its course, unless complications are present. And quinine given with patient at perfect rest will control all symptoms within five days, if the attack is at all amenable to treatment; if not amenable to treatment, death will be so prompt that there will be no time to hestitate over diagnosis.

The most important point to remember in the study of malaria is the large number of infections that may be present along with an acute malarial infection. A lack of the knowledge of this fact, no doubt, accounts for the confusion in our ideas with regard to the course of malaria, and its non-amenability, in exceptional instances, to treatment.

Finding malarial parasites in the blood is not the end of the diagnosis, but just the beginning.

When quinine is given properly and fails to have a marked effect upon the fever in forty-eight to sixty hours, although parasites may be present in the blood, there is some complication; and when in an acute malarial infection the fever is once reduced by quinine, and there is again a rise of fever, all treatment remaining the same, the second rise is not due to malarial infection, but to some underlying condition aroused to activity, or to an intercurrent infection manifesting itself late in the malarial attack.

Diagnosing a fever that persists over five days in spite of quinine, as 'clinical malaria," is not justifiable.

Leucocytoses from inflammatory diseases are inimicable to the development of the malarial parasite. In the presence of a marked leucocytosis, the idea of malarial infection should be abandoned, and search made for the cause.

When we are in malarial climates, if we will but bear these few facts constantly in our minds, and govern ourselves accordingly, we shall be the means of great comfort to our patients; the means of preventing unnecessary loss of life by too long neglect of tuberculosis, deep-seated suppuration, and often sepsis; and finally, be the means of preventing the spread of useless and unnecessary epidemics.

Appendix: January, 1909, Report Department of Health. C. Z.

BOARD OF HEALTH LABORATORY, ANCON, C. Z.

Observations have been made on the rate of decrease of the sexual forms of malaria parasites in patient's blood as influenced by quinine and rest in hospital, and it has been determined that the sexual or transmitting forms of the parasite may be reduced by quinine and rest to a number insufficient to infect a susceptible Anopheles mosquito. In most cases this can be accomplished with quinine—10 grains three times a day—within ten days.

(8) Research by Dr. Samuel T. Darling, Chief of Lab.

[1] Tropical Diseases, 4th edition, Manson.

[2] Relapsing Fever, report by Dr. Walter V. Brem.

[5] Atypical Typhoid Fever, *Journal A. M. A.*, February 22, 1907.

[7] Lane Lectures on Tropical Diseases, 1905, San Francisco—Manson.

[6] Clinical Malaria, Analysis 500 Cases, Dr. Nelson D. Brayton.

[3] Pathological Records, Ancon Hospital, 1908.

[4] Atypical Typhoid Fever, Result of Blood Cultures, *Journal A. M. A.*, April 3, 1909.

Reprinted from the New York Medical Journal for May 1, 1909.

Discussion.

Dr. WILLIAM S. THAYER, of Baltimore, said that he was astonished that Dr. Bates should make the statement that the malarial parasites were not found in any greater number in the internal organs than in the peripheral blood. He considered this a strange statement from one who had had such opportunities for observation as Dr. Bates. Dr. Thayer said that one not infrequently found a moderate number of parasites in the peripheral circulation and an enormous number in the internal organs—the brain, the spleen, or the bone marrow. A red corpuscle containing a parasite of any size was often more in the nature of a foreign body than of a red corpuscle, as could be easily seen in fresh blood: and one would expect that corpuscles so changed and shrunken as those in æstivoautumnal malaria or as the swollen cells in tertian malaria would be retained, in great part, in the bone marrow and other internal organs. There were occasionally cases of severe infections with malarial fever in which there were no parasites found in the peripheral circulation, even with the most careful staining. He referred to such a case that he had seen recently. The spleen was enlarged and paroxysms occurred. The spleen was not aspirated; but no parasites of any kind were found in the peripheral circulation, though stained specimens were made. Upon the administration of quinine, the fever immediately disappeared, and the evidence was very strong that this was a case of malaria in which parasites were absent from the peripheral circula-

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tion. Dr. Thayer said that it was impossible for him to believe that, unless parasites had been present in great numbers, they could have produced such severe symptoms.

He had seen several cases in which tuberculosis exactly simulated malaria, but in which the blood showed no parasites, the existence of tuberculosis having been demonstrated by an examination of the sputum. He had also encountered cases of trichiniasis resembling malaria most markedly. The paroxysms were like those of æstivoautumnal infection. Embryos were discovered in the muscles of the leg. There was a history of œdema of the eyelids at the outset of the attack, and there was no reason to believe that malaria existed.

Dr. George Dock, of New Orleans, said that the circulation did not go on in a series of tubes without an outlet; it was like the circulation in a city water supply. When the faucets were opened, the current changed; and when there were outlets into the spleen and other organs, there were modifications in the peripheral blood stream. He had himself reported a case in which he was unable to find parasites in the circulating blood, yet found enormous numbers of them on puncturing the spleen; and he thought that the fact that this frequently occurred must be accepted.

In regard to Dr. Bates's remark about intoxication, Dr. Dock said that he did not believe it to be necessary to have a large amount of toxic substance present in order to produce symptoms of intoxication. In suppurative middle ear disease or appendicitis, in which bacteria grew under special conditions, they produced toxines of great potency; and in malarial fever there were other factors at work, such, for instance, as susceptibility. He did not think that the idea of a toxic origin could be given up on the grounds advanced by Dr. Bates.

In regard to treatment, Dr. Dock was glad that Dr. Bates considered that the majority of cases of malaria could be checked in forty-eight hours, as he himself had held that Dr. Osler's limit of five days was too long. He thought it would be well to ask those that believed in the "therapeutic test" to confine themselves to forty-eight hours, as cases existed in which paroxysms continued for several days after the patients were filled with quinine. Dr. Dock believed the "therapeutic test" to be a poor guide. He thought that one should use the microscope and, if necessary, puncture the spleen, although care should be taken in the latter manipulation.

Reprinted from the New York Medical Journal for July 3, 1909.

QUARTAN MALARIA COMPLICATING CHRONIC PARENCHYMATOUS NEPHRITIS, ÆSTIVO-AUTUMNAL MALARIA COMPLICATED BY BRONCHOPNEUMONIA.*

By John M. Swan, M. D.,
Philadelphia,
Instructor in Tropical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine.

(*From the Polyclinic Laboratories.*)

The case of quartan infection is of interest because it was accidently discovered in a patient admitted to the Polyclinic Hospital, in the service of Dr. A. A. Eshner for nephritis. When it was learned that the man had recently landed in Philadelphia from Jamaica, his blood was studied and was found to contain a single generation of quartan parasites. The patient had not had a chill, but his temperature had registered 99.4° F. at 8 a. m. on October 9th. Seventy-two hours later the temperature registered 100.4° F., without a chill; and at the next seventy-two hour period there was a chill, and the temperature reached 101.4° F. On this date an examination was made to determine the relation of the formation of the segmenting forms of the parasite to the paroxysm. The paroxysm was due, according to our calculations, on the 15th at 8 a. m. At 10 p. m. on the 14th the blood contained presegmenting bodies and a few rosettes. at 2 a. m. on the 15th it contained rosettes, presegmenting bodies and small rings. At 4 a. m.

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*Read at the sixth annual meeting of the American Society of Tropical Medicine, held in Washington, April 10, 1909.

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it contained small rings, rosettes, and gametocytes. At 6 a. m. it contained small rings and gametocytes. At 8 a. m. it contained small rings in moderate numbers. It would appear from the results of this examination that the paroxysm in quartan infection does not follow sporulation so closely as it does in the benign tertian infection.

The nephritis in this case was considered to be independent of the malarial infection, because the cure of the latter had no influence on the former. The return of the dropsy, with chest pain, chills, cough, and blood tinged expectoration, from which the patient died, was unaccompanied by the recurrence of the sporulating parasites in the peripheral blood; and examination of the bone marrow after death failed to show malarial pigmentation.

The relation between malarial infection and nephritis has been thoroughly studied by Thayer.[1] As a result of the analysis of 758 cases of malarial fever seen in the Johns Hopkins Hospital, Thayer concluded, first, that albuminuria is a frequent occurrence in the malarial fevers of Baltimore, having been found in 46.4 per cent. of the cases. Second, that albuminuria is more frequent in cases of infection with the malignant tertian parasite than in infections with the other parasites. In the former albuminuria was found in 58.3 per cent. of the cases; in the latter in 38.6 per cent. of the cases. Acute nephritis occurred in 2.7 per cent. of the cases treated in the hospital wards, and in between 1 and 2 per cent. of all cases seen. Third, that the frequence of albuminuria and nephritis in malarial fever, while somewhat below that observed in the more severe acute infections, such as typhoid fever, scarlet fever, and diphtheria, is considerable. Fifth, that there is reason to believe that malarial infection, especially in the more tropical countries, may play an appreciable part in the ætiology of chronic renal disease.

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[1] *American Journal of the Medical Sciences,* November and December, 1898.

Case I.—The patient was a negro, male, aged twenty-three years, who was admitted to the Polyclinic Hospital (No. 14,703) on October 7, 1907, complaining of "cold headache" and pain "all over his body."

There was nothing of importance in his family history.

Past History.—He had had whooping cough and chicken-pox in infancy, and smallpox when he was seven years old. He denied syphilis. He had an urethral discharge two years before. On two occasions, five years before and three years before, he said that he had had attacks similar to the present one, characterized by marked swelling of the face and feet, of the trunk to less extent, and severe headaches. He said that these attacks followed "taking cold." He was born in Jamaica, and came to to the United States from the West Indies six months before.

History of the Present Condition.—The patient had been ill for one week with the symptoms as described. His face, feet, and abdomen commenced to swell, and these symptoms had continued. He had had three watery bowel movements daily for the last week. On examination the patient was found to be a well developed negro male. His face, eyelids, chest, and abdomen were œdematous. There was no œdema of the legs. The tongue and mucous membranes were pale. The conjunctivæ were pale but there was no jaundice. The lungs were negative. The liver and the spleen could not not be palpated. The heart was not enlarged to percussion. Its apex was visible and palpable. There was an impurity in the systolic sound at the apex; but no accentuation of the second aortic sound. The abdomen was much distended and was dull on percussion. It seemed somewhat tender on palpation. A distinct though slight fluid wave could be felt on bimanual examination. The scrotum was œdematous. The patient was stupid and rather surly. An examination of the urine showed: Reaction, alkaline; color, pale straw; specific gravity, 1.012; albumin, 0.4 per cent. (Esbach); no glucose. There was a slight flocculent sediment which was composed of pus cells, granular casts, and renal epithelium. A second urine analysis showed: Reaction, acid; specific gravity, 1.012; albumin, 0.4 per cent. (Esbach); no glucose. There was a white

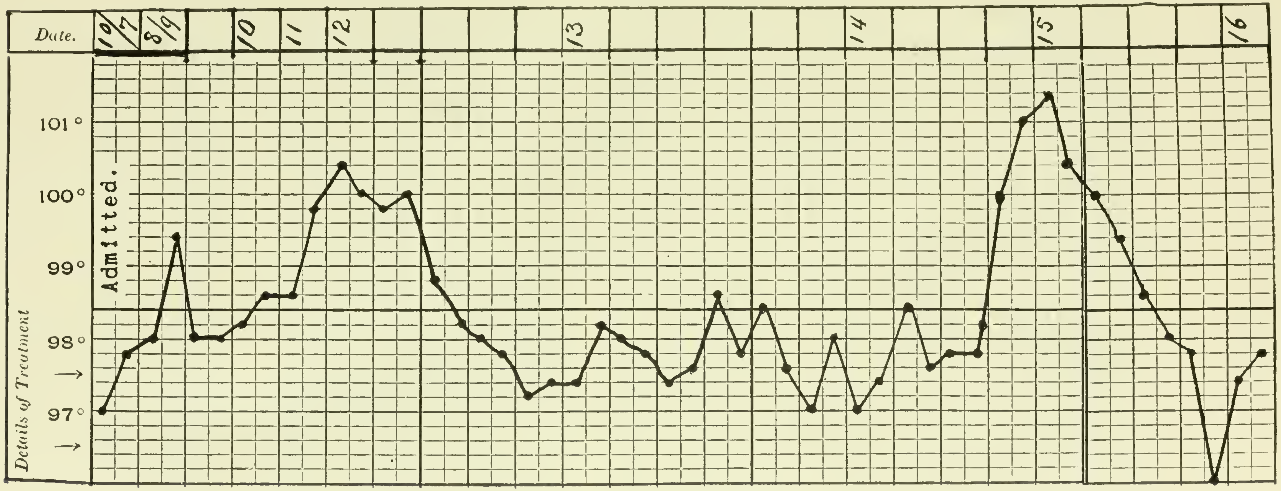

CHART I.—Case of quartan malaria.

sediment composed of numerous dark and pale granular, epithelial, and leucocytic casts, red blood corpuscles, pus cells, and renal epithelium. A blood examination showed: Erythrocytes, 2,750,000; leucocytes, 8,400; hæmoglobin, 35 per cent. (Dare); ratio, 1 to 327; color index, 0.63 +. Differential leucocyte count, polymorphonuclear neutrophiles, 62.6 per cent.; lymphocytes, 16.2 per cent.; large mononuclears, 15.8 per cent.; transitionals, 0.6 per cent.; eosinophiles, 4.4 per cent.; myelocytes, 0.4 per cent. There was marked anisocytosis and granular degeneration of the erythrocytes. In counting 500 leucocytes, 59 quartan parasites were found (*Plasmodium malariæ*).

Examination of the fæces showed a few ova of trichocephalus trichiuris. The œdema of the scrotum had disappeared on October 11th. On the 12th a urine analysis showed: Total quantity for twenty-four hours, twelve ounces +; reaction, acid; color, straw; specific gravity, 1.016; albumin, 0.4 per cent. (Esbach). Numerous pale and dark granular casts, and renal epithelial cells. On October 13th the œdema of the face, eyelids, and trunk had diminished. A urine analysis showed: Total quantity for twenty-four hours, thirty-four ounces; reaction, slightly acid; color, pale straw; specific gravity, 1.012; albumin, 0.35 per cent. (Esbach). There was a fine flocculent sediment, which contained granular casts, epithelial cells, amorphous phosphates, and urates. On October 14th, the patient had a chill with a temperature of 101.2° F. at noon. Examination of the urine showed: Total quantity for twenty-four hours, sixteen ounces; reaction, feebly acid; color, pale straw; specific gravity, 1.012; albumin, 0.35 per cent. (Esbach). There was a fine flocculent sediment, which contained granular and epithelial casts, pus cells, and epithelial cells. The casts seemed fewer in number than on previous examinations. On October 15th the œdema was less, and the patient said he felt better. He had two large yellow stools. A urine analysis showed: Color, straw; specific gravity, 1.012; albumin, 0.35 per cent. (Esbach); granular and epithelial casts and leucocytes. Total quantity for twenty-four hours, twenty-five ounces.

On October 21st urine analysis showed: Reaction, acid; color, straw; specific gravity, 1.012; albumin, 0.31 per cent. (Esbach); pus cells, epithelial cells, amorphous urates, and granular casts. Total quantity in twenty-four hours, thirty-one ounces. Œdema greatly lessened, noticeable to slight extent only around eyes and face. Stools varied from two to four daily. Slept well. There had been no rise of temperature above normal since October 14th.

On October 25th urine analysis showed: Reaction, acid; color, pale straw; specific gravity, 1.014; albumin present; no glucose; there was a slight flocculent sediment composed of granular and epithelial casts, pus cells, and epithelial cells.

On October 31st urine analysis showed: Reaction, acid; color, pale straw; specific gravity, 1.012; albumin, 0.3 per cent. (Esbach). There was a fine flocculent sediment which contained granular and epithelial casts, pus cells, and epithelial cells. A blood count showed: Erythrocytes, 2,144,000; leucocytes, 8,000; ratio, 1 in 268; hæmoglobin, 35 per cent. (Dare); color index, 0.81 +. A differential count gave polymorphonuclear neutrophiles, 67.4 per cent.; lymphocytes, 23.0 per cent.; large mononuclears, 3.6 per cent.; transitionals, 0.6 per cent.; eosinophiles, 4.8 per cent.; and basophiles, 0.6 per cent. One degenerated gametocyte was seen in counting 500 leucocytes.

On November 5th the urine analysis showed: Total quantity for twenty-four hours, forty ounces; reaction, alkaline; color, pale straw; specific gravity, 1.012; albumin, 0.3 per cent. (Esbach); no glucose. There was a fine flocculent sediment which contained pale and dark granular casts, triple and amorphous phosphates, ammonium urate crystals, few epithelial cells, and pus cells. The patient complained of no insomnia, headache, nor other discomfort; his bowels moved freely; the œdema was still present about his eyes but was not noticeable elsewhere. He was discharged.

He was readmitted to the hospital on November 24th (No. 14,897), complaining of pain in left lower axillary region, at times sharp, which he had noticed for two weeks. He also complained of discomfort in the epigastrium. He had had eight or ten chills since November 5th, and had been confined to bed most of the time. He had had a moderate cough for two weeks, with a moderate amount of sputum, which, he said, was blood streaked at times. He had usually been drowsy. His bowels moved from one to three times daily. He thought the daily amount of urine passed was normal, and that the swelling of his face had increased.

On examination, the œdema of the face was found to be marked. The mucous membranes were pale. There was a faint systolic murmur heard at the base and at the apex of the heart, which was not transmitted. There was no cardiac enlargement. The patient had cough with considerable amount of expectoration which, however, contained no blood. Moist râles were heard on both sides of the chest.

Urine analysis showed: Total quantity in twenty-four hours, ten ounces; reaction, alkaline; color, straw; specific gravity, 1.016; albumin, 0.6 per cent. (Esbach); no glucose. There was a fine flocculent sediment which contained hyaline and granular casts, phosphates, epithelial cells, and leucocytes. No malarial parasites were found in the blood.

Examination of the blood showed: Erythrocytes, 3,008,000; leucocytes, 9,800; ratio, 1 in 308; hæmoglobin, 30 per cent. (Dare); color index, 0.49 +.

On November 27th he complained of headache and general muscular pains. He had a chill with a rise of temperature to 104.4° F., but no malarial parasites were found.

On November 28th, urine analysis showed: Total quantity for twenty-four hours, twelve ounces; reaction, acid; color, straw; specific gravity, 1.022; albumin, 0.1 per cent. (Esbach); no glucose. There was a turbid sediment which contained numerous hyaline, pale and dark granular casts, pus and epithelial cells.

On November 29th a blood examination again showed no malarial parasites. It was thought that the elevation of temperature was due to nephritis. The cough was much improved. No urine had been passed and the catheter failed to get any. The bowels had moved freely. The patient was in a stupor most of the time. He had no twitching, no convulsions, and no headache.

He continued in stupor until the 1st of December. On that date his pulse became very feeble; Cheyne-Stokes respiration appeared, and he died at 10:45 a. m.

The body of this patient, being unclaimed, went to the Pennsylvania Anatomical Board. The body, fortunately, was afterwards sent to the dissecting room of the Polyclinic Laboratories, where through the courtesy of Dr. Addinell Hewson, professor of anatomy, I was given a chance of examining the liver, the spleen, and the bone marrow. No evidence of malarial infection was found in these organs.

The case of astivoautumnal infection was in the person of a male, aged forty years, who was mate on a sailing vessel in the coasting trade. He was admitted to the Polyclinic Hospital in the service of Dr. A. A. Eshner, complaining of hiccough. He had a remittent temperature, which appeared to indicate infection with a subtertian parasite of twenty-four hour cycle of development. No suspicion of malarial infection was entertained, and consequently the only hæmatological examination

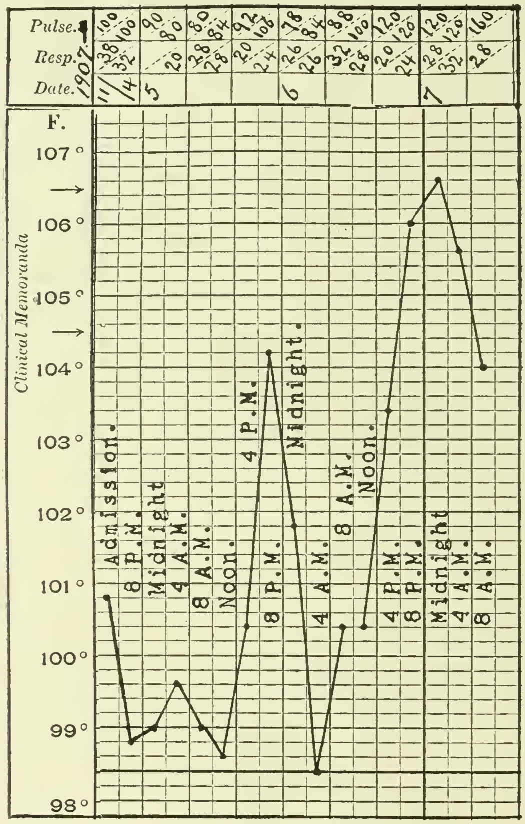

CHART 2.—Case of æstivoautumnal malaria.

made during his stay in the ward was the routine cell count and hæmoglobin determination done by the resident physician. At autopsy the very large spleen suggested the nature of the disturbance, and smears made from the expressed spleen pulp showed a large number of pigmented

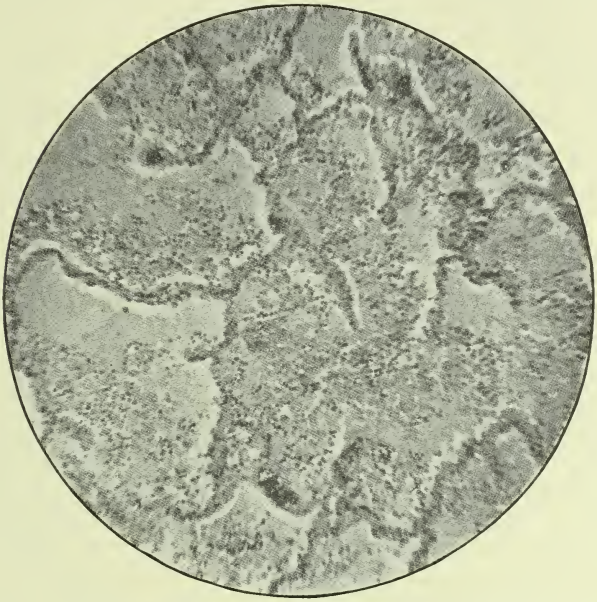

Fig. 1.—Bronchopneumonic area of lung. Case of æstivoautumnal malaria. (Zeiss obj. AA, ocular 6 apochromatic.)

macrophages and a fair number of deformed and partly degenerated parasites. The chief interest lies in the bronchopneumonia. During life there were no symptoms which pointed to pneumonia. To the naked eye the lung looked to be merely affected by the ordinary hypostatic congestion. On histological examination, however, a true pneumonic consolidation was seen. The exudate was not that of a true pneumococcus infection, consisting of erythrocytes, polymorphonuclear leucocytes, granular matter, and

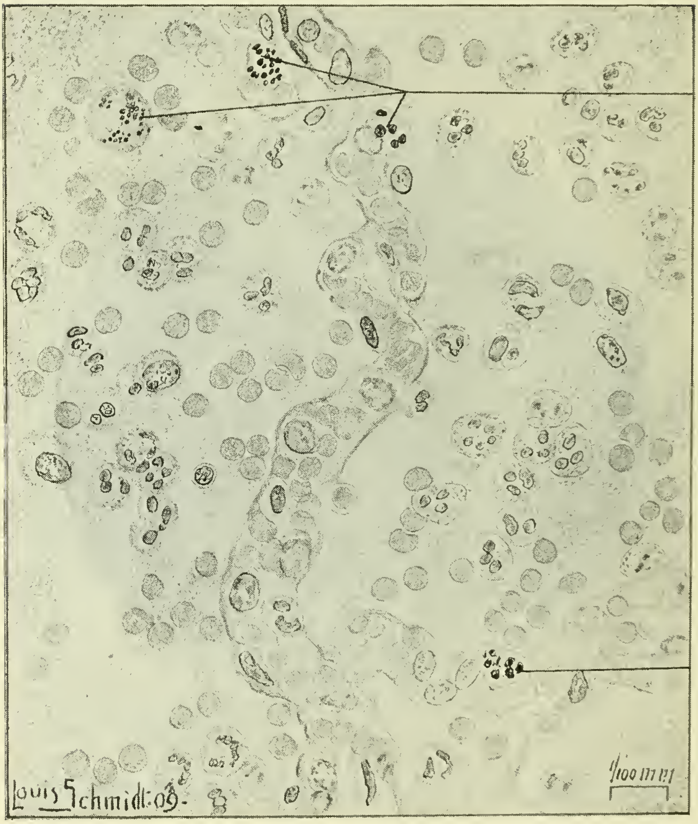

FIG. 2.—Bronchopneumonic area of lung, showing anatomical character of exudate. *a, a,* macrophages containing malarial pigment.

large uninuclear cells containing malarial pigment. Special staining methods failed to show more than a few small masses of fibrin and no Gram positive organisms. The macrophages may be accidental in the exudate, but the question of their relation to the pneumonic process was suggested.

Mannaberg[2] is of the opinion that all types of malaria may be complicated with croupous pneumonia and that the pneumonias are always examples of mixed infections. The complication of acute malaria with pneumonia is not frequent; but, in regions in which malaria is endemic, an epidemic of pneumonia may occur at the time of a malarial epidemic and then both diseases will be seen in association. The subjective symptoms are usually marked; they increase on the occasion of an intercurrent malarial paroxysm, the three phases of which may sometimes be recognized. The objective signs of the pneumonia are not altered, whether or not a malarial paroxysm is in progress, and these continue until the pneumonia has passed. The sputum is usually markedly hæmorrhagic, and shows sometimes, besides the *Diplococcus pneumoniæ* malarial parasites which have passed into the sputum with the blood corpuscles. Mannaberg denies the existence of a condition such as that described by de Brun.

Thayer and Hewetson[3] found pneumonia in two out of the 616 cases upon which their monograph was based. Both were cases of typical croupous pneumonia in patients with benign tertian infections, and both ended in recovery. In neither did the pneumonia show anything remarkable in its course, nor is it likely that the malaria exerted any influence upon the pneumococcus infection, excepting in so far as it may have prepared the soil.

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[2] *Nothnagel's Practice,* American Edition.
[3] *The Malarial Fevers of Baltimore.*

In 1895, H. de Brun[4] described twenty-seven cases in which there were symptoms pointing to pulmonary tuberculosis. The signs indicated the existence of a temporary condensation of the lung. There were no localizing signs of inflammation or of a catarrhal change in the alveoli. There were no signs of bronchial inflammation, no signs of pleural inflammation, and no tubercle bacilli were found in the sputum. In one fatal case the lung had the gross appearance of bronchopneumonia; in another fatal case the lungs were sclerotic and pigmented; and in the other fatal cases the lungs were normal. Twenty-three of the patients recovered. De Brun believed these cases to be due to malarial infection. In 1901, Naame[5] confirmed the observations of de Brun. He asserted that he had seen a number of cases in which there was solidification of the apex of one or of both lungs. This consolidation was accompanied by a certain degree of dulness with resistance to the finger, augmentation of vocal resonance, and bronchophony. The cough, when it existed was dry and usually coincided with the attack of fever. The most important sign, however, was the absence of any adventitious sound except an expiratory wheeze.

In the case under review it appears to me that we have a pneumonia which is not of the ordinary type mentioned by Mannaberg and by Thayer and Hewetson, nor of the type described by de Brun. I am of the opinion that the bronchopneumonia in this case was due to the irritation of the malarial pigment on the lung tissue.

Case II.—The patient was an unmarried male, aged forty years, who was admitted to the Polyclinic Hospital (No. 14,814) on November 4, 1907, suffering from severe hiccough.

There was nothing of interest in his family history, except that his father had died of tuberculosis. He had had the usual diseases of childhood, and an attack of gonorrhœa five or six years before his admission. He was a sailor on a coasting vessel, and had made his last cruise from Savannah, Ga., to Philadelphia.

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[4] *Revue de médecine,* 1895, pp. 361 and 929

[5] *Revue de médecine,* December, 1901.

The attack developed rather suddenly about fourteen days before admission. He at first felt weak and indisposed. This continued for two or three days and then the hiccough commenced. He had had periods of one or two days at a time during which there was no hiccough. He complained of nothing at the time of admission except weakness. He knew of no exciting cause for his complaint. He slept poorly and he had lost weight. The urine analysis gave the following result: Reaction, alkaline; color, red amber; faint trace of albumin; no glucose. There was a heavy white sediment, which was composed of phosphates and ammonium urate crystals, and epithelial cells. An incomplete blood count, made by the resident physician on duty at the time, showed 3,690,000 erythrocytes; 15,000 leucocytes; and sixty per cent. hæmoglobin by the Dare instrument. The agglutination test with bacillus typhosus was negative. The hiccough continued with very few intermissions until the patient's death, on November 7th. He became progressively more emaciated and exhausted. Twelve hours before death his temperature registered 106.4° F. in the rectum; his pulse was 120 per minute; and his respirations were 28 per minute. Nine hours before his death he vomited, and attacks of vomiting were frequent until death, which occurred at 9:00 a. m. One hour before death his temperature was 104° F., pulse 160, and respirations 28 per minute.

Necropsy.—Anatomical Diagnosis: Old adhesive pleuritis. Hypostatic congestion and œdema of the lungs. Atheroma of the mitral valve. Atheroma of the aorta. Cloudy swelling of the kidneys. Acute splenic tumor. Active congestion of the liver. Acute malarial fever (æstivoautumnal).

Histological Diagnosis: Cloudy swelling of the liver. Active congestion of the liver. Malarial pigmentation of the liver. Active congestion and cloudy swelling of the kidneys. Malarial pigmentation of the kidneys. Malarial pigmentation of the heart muscle. Congestion of the spleen. Malarial pigmentation of the spleen. Bronchopneumonia, œdema of the lungs; malarial pigmentation of the lungs.

The body of a white male adult; weight, 160 pounds; height, six feet. The bony skeleton was large; the musculature was wasted; the skin was sallow; the panniculus adiposus was slight. Post mortem rigidity was absent; post mortem lividity was present about the neck and in the dependent parts. There was a small scar on one knee. The preperitoneal adipose tissue was slight; the abdominal muscles were of good color, and were somewhat emaciated.

Abdominal cavity: On opening the abdominal cavity the liver was seen projecting four inches below the costal margin. The bladder was distended with urine and projected two inches above the brim of the pelvis, otherwise the contents of the abdominal cavity were in their normal positions and relations. The diaphragm rose to the fifth interspace on the right side, and to the sixth interspace on the left side.

Thoracic cavity: On opening the thoracic cavity the organs were seen in their normal positions and relations. The sternum was normal; the costal cartilages were calcified. The left pleural cavity contained a few dense, old adhesions between the anterior border of the lung and the region of the fourth rib. There were a few dense adhesions between the posterior surface of the right lung and the thoracic wall. Lungs: The left lung was normal in size. The pleural surface was glistening, transparent and pale. On section the surface was granular, dull, and mottled with dark red particles. Crepitation was lessened. On pressure the lower lobe of the organ exuded a large quantity of frothy, blood stained serum. The right lung was normal in size. The lower lobe and the dependent portion of the middle lobe were pink in color. On surface the section was mottled with dark red patches. Crepitation was lessened. On pressure the organ exuded a quantity of frothy, blood stained serum. Heart: The pericardium was normal. There was a milk spot on the anterior surface of the right ventricle. The heart was normal in size and position. The subpericardial adipose tissue was normal in amount. The left side was distended with fluid blood. The mitral orifice admitted two fingers; the tricuspid orifice admitted three fingers. The aortic, pulmonary, and tricuspid valves were normal. There were a few small atheromatous ulcers on the aortic leaflet of the mitral valve. The wall of the left ventricle, and that of the right ventricle were normal. The heart muscle was normal in color, and firm in consistency. The arch of the aorta was distended with blood.

Kidneys: The left kidney was slightly enlarged. It was pale in color. The cortex was thicker than normal; the medulla was thinner than normal. On section the surface was smooth, pale, and of normal consistence. The left adrenal body was normal in appearance. The right kidney was slightly enlarged. On section the surface was smooth, pale in color, and of normal consistence. The cortex was increased in thickness; the medulla was thinner than normal. The right adrenal body was not examined.

Spleen: The spleen was much enlarged. It was increased in consistency. The capsule was normal in thickness. On section the surface presented a very dark red color; it was smooth and firm. The pulp was increased in consistency; the follicles were not distinguishable; and the trabeculæ were increased in number and size.

Liver: The liver was much enlarged. It was of normal shape and of increased consistency. The surface was smooth; the edges were rounded; the capsule was normal. On section the surface was dull, moist, granular, and opaque. The organ was of a slate gray color, and the amount of blood in it was much increased. The gallbladder was filled with inspissated bile. Its mucous membrane and its walls were normal. The bile ducts were patulous. The lymphnodes in the transverse fissure were slightly enlarged.

Bladder: The bladder was distended with urine; otherwise it was normal. The external genitalia were normal.

Gastrointestinal Tract: The omentum was normal in size, shape, and position. It was devoid of fat. The stomach was normal in position and size. It contained a small quantity of dark brown fluid. Its walls and mucous membrane were normal. The small intestine showed congestion in the duodenum, a gray, thickened mucous membrane in the jejunum; and a few erosions in the ileum. The appendix was rather long; but was otherwise normal. It was furnished with a mesoappendix to its tip. The colon was slightly congested. The rectum was normal. The retroperitoneal lymphnodes were slightly enlarged.

Pancreas: The pancreas appeared normal.

Aorta: The thoracic and abdominal aorta presented a few atheromatous ulcers.

Histological Examination.—Liver: The liver was congested, particularly in the intralobular capillaries. The interlobular vessels were less markedly distended, while the intralobular vein was in most instances empty. The amount of blood between the liver cells was considerable, as was particularly shown in a specimen fixed in alcohol, in which many of the blood corpuscles had been washed out of the capillaries. The hepatic cells were somewhat swollen, the nuclei did not stain well, and the cytoplasm was finely granular. There were many cells containing rounded masses of nearly black pigment of varying sizes. These cells were particularly numerous in the capillaries; but they were also present in the larger sized vessels. They were always large uninuclear elements, evidently the endothelial cells of the vessels. No yellow pigment was seen, no distinct malarial parasites were seen.

Kidney: The kidney was congested, but not uniformly so. The tubules, for the most part, were quite normal, although there was some swelling of the renal epithelium. There was little pigment present, which was to be seen in the glomeruli.

Heart Muscle: The heart muscle was quite normal in appearance. The blood vessels were congested. There were a few cells containing fine pigment in the vessel walls.

Spleen: The spleen was extremely congested. The Malpighian bodies were indistinctly visible, and were extensively pigmented. The lymphocytes of the Malpighian bodies were very intimately mixed with red blood corpuscles. There was a great amount of pigment in varying sized globules in the splenic pulp, and in the Malpighian bodies, always contained in the large uninuclear cells. There were a few polymorphonuclear leucocytes in the pulp, and some cells with nuclei showing mitoses. No distinct parasites were seen.

Lung: The lung presented numerous patches of consolidation. The exudate was composed of granular matter, red blood corpuscles, large uninuclear cells containing fine pigment granules, and polymorphonuclear leucocytes. Some of the macrophages were apparently lining epithelial cells of the air vesicles. The lung was uniformly congested, and there was a moderate number of macrophages in the blood vessels. Sections of the lung stained by the Mallory aniline blue[6] method showed a very few small masses of fibrin in the alveoli and in the bloodvessels. Sections stained by the Gram-Weigert method failed to show Gram positive diplococci or bacilli.

Smears made from the spleen pulp at autopsy showed large numbers of macrophages containing various sized granules of black malarial pigment. There were very few polymorphonuclear cells in the smears. A few distorted gametocytes were seen, and a few bodies in the red blood corpuscles that looked like small unpigmented rings. The length of time between death and the preparation of the specimen would account for the lack of more positive information.

Bacteriological observations: Culture tubes of agar were inoculated from the spleen, the liver, and the kidney. All were sterile after forty-eight hours' incubation at 37.5° C.

I wish to take this opportunity to thank Dr. Eshner for permission to study and report these cases.

3713 WALNUT STREET.

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[6] Mallory and Wright. *Pathological Technique.*

Reprinted from the New York Medical Journal for May 1, 1909.

Discussion.

Dr. C. C. Bass, of New Orleans, said that he had had a case of quartan malaria similar to the one reported by Dr. Swan. There were few or no symptoms. The patient had been infected five months previously, and had had chills and fever, which responded occasionally to quinine and then recurred. When the patient came into the hospital he had a temperature of 101.5° or 101° F., but most of the time the temperature was normal or subnormal. After he had been in the ward three or four days, twenty grains of quinine were given him through mistake. He had previously shown three crops of parasites and had had irregular periods of chills and fever. The administration of quinine was stopped as soon as the error was discovered. The plasmodia were absent the next day, and from that time on, until a month and a half later, he had no more parasites. He was then discharged, though not perfectly well, no satisfactory explanation for his condition being apparent. He returned to the hospital about a month later, two months and a half from the time that he had had parasites in his blood. Quinine was given him, but no plasmodia could be found. He died about a month afterward, never having had fever or shown parasites, and the autopsy disclosed tuberculous peritonitis. The spleen failed to reveal parasites on post mortem examination. The case was not an old infection in which the patient had got so accustomed to the malarial condition that he had stopped having fever, for he had not been infected more than five months, the history being very definite on that point. Dr. Bass laid stress upon the fact that the patient had had three crops of

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parasites, and that he had received but one dose of quinine and some calomel, nothing else having been given; yet that he had got rid of his parasites and had shown none afterward.

Dr. THAYER referred to a case of quartan malaria that he had seen at Johns Hopkins Hospital a number of years ago. The patient died within a short time after treatment, and showed remarkably few evidences of malaria at the autopsy. He also referred to a case of the obstinate type of quartan malaria in a man who had consulted Dr. Osler on account of recurrent chilis from which he had been suffering for two years. Dr. Osler did not think the case was one of malaria, but Dr. Thayer found quartan parasites. After treatment with quinine for a week or ten days the patient was well enough to return to business.

Dr. BASS related two other cases of quartan malaria that had occurred at the Charity Hospital in New Orleans. One was in a patient who had lived in Honduras for two years, and had had chills and fever. He paid no attention to it. On admission, he showed an enlarged spleen and an infection, with three crops of quartan parasites. As soon as quinine was given him the parasites immediately disappeared from his blood. Quinine was discontinued at the end of three days, but although he was kept in the ward ten days longer and the spleen remained enlarged, no more parasites could be discovered.

Dr. Bass said that quartan malaria was very rare in his section of the country. The pathologist at the Charity Hospital, however, thought that he could recognize a different type of plasmodium in the patients coming from Honduras, and had named it the Honduran malarial parasite. The case related by Dr. Bass was one of these cases, and the pathologist had made the diagnosis in this instance without knowing where the patient had come from. Although Dr. Dock and other had studied slides from these cases and from others that had not come from Honduras, they were of the opinion that no such distinction could be made. The rosette of the Honduran type of quartan showed from eight to nine spores, and the reduction in the size of the red corpuscle as the organism developed was perfectly typical. Although a good deal of fine and pretty active pigment was found, it was, as general rule, the coarse pigment of the quartan type.

In another case which occurred in the same hospital the diagnosis was made from the history, without microscopical confirmation. This patient came from Alexandria, La. He gave a clear history of quartan malaria, but had no paroxysms while in the hospital.

Dr. Dock said that the cases of Honduran fever in the Charity Hospital had not been allowed to go untreated, and, therefore, that the type of fever was not determined. He confirmed what Dr. Bass had said about the diagnosis of the organism from that locality, it having been made without the type of the fever being known. He thought that one explanation why the diagnosis of quartan malaria was not made was that a number of the patients had not been allowed to furnish proper temperature charts, and said that the old English idea of the greater severity and obstinacy of quartan malaria did not always hold good. In a case of quartan malaria reported by him some years ago, the patient was easily cured by a single dose of quinine.

Dr. Dock then referred to the enormous number of parasites that had been found in Dr. Bass's second case, several segmenting bodies having often been found in every field; yet the patient had died without showing marked symptoms. There was also a very decided æstivoautumnal infection, a crescent having been found later on.

Discussion.

Dr. O. T. Logan, of Changteh, China, said that the recovery of the patient mentioned by Dr. Bass was easily explained, that being the way in which our forefathers got well before the discovery of quinine. While in China, Dr. Logan had observed cases of malaria in persons who refused to take medicine. By going to bed they would get rid of their fever and eventually recovered; but as soon as they got up the symptoms would recur. Eventually, however, they would get rid of the disease entirely. This same fact, he thought, accounted for the immunity from malaria enjoyed by the natives of Africa.

Dr. Henry Skinner, of Philadelphia, said that a distinct species or a geographical race of malarial parasites might be expected from analogy to other forms of life. Whenever there was a wide geographical range of distribution, changes in morphology existed, so that it was often possible for a naturalist to say whence an individual came. Even though certain individuals were considered to belong to the same species, it was possible to distinguish a European from an American specimen. Dr. Skinner believed that the Honduran parasite might be either another species or a distinct geographical race.

Dr. W. P. Chamberlain, of Jackson Barracks, La., said that in an investigation made by him four years ago the anopheles had been found to constitute seven per cent. of all mosquitoes in that locality. In studying malaria he had found that four patients resisted the administration of quinine by the mouth for four days, but that all others promptly yielded to this treatment. Among the latter were four cases of quartan malaria, which yielded as quickly as the others. None of the quartan cases relapsed, whereas many of the others did or the patients became reinfected a few months after the original attack.

Reprinted from the New York Medical Journal for August 7, 1909.

A STUDY OF THE LEUCOCYTES IN TROPICAL MALARIAL INFECTIONS.*

By Paul T. Talbot, M. D.,
New Orleans, La.

Of recent years our attention has been called to the study of various tropical diseases. Our researchers and investigators have realized that in them we are dealing with peculiar manifestations often seen in our section of the country and until recently little understood. Since the marked increase of work in that direction new diseases and valuable information unthought of have been given to the medical profession.

During my service in the medical wards of the Charity Hospital my attention was repeatedly called to a group of malarial cases, which on account of their peculiar history and marked anæmia suggested to me a necessity for careful study. All these patients had seen recent service in and around Central America, the majority coming from Spanish Honduras and giving history of ague, but known, or called by physicians and laity of their locality, tropical anæmia.

Beginning with these observations I was able to follow nine cases in my wards. Subsequently I collected fifteen more; nineteen of the total I have observed personally, the others collected from the records of the Charity Hospital.

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*Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10, 1909.

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On careful study I was immediately impressed with the relative white blood count of such cases which showed a constant increase of the small lymphocytes; contrary to previous teachings on malaria, coupled also with a very erratic form of plasmodium.

The mosquitoes are very numerous in the states of Central America, and the ordinary layman at work has no protection from their bites. Entering Central America as healthy individuals, some would receive the infection early, others later. They would begin to have chills and fever, associated with a severe anæmia and rapid loss in flesh, some losing forty to fifty pounds in the course of a few weeks showing that a severe toxæmia existed. This anæmia is very marked, and in the earlier cases led me to believe that patient had primary anæmia. Only one out of the number had any previous malarial infection, this being three years previous to the present infection, the majority of the patients being very healthy and hearty individuals before infection.

A great amount of physical depression existed and in the most virulent cases some mental hebetude. During their stay in the tropics they would usually try by antimalarial treatment to relieve their symptoms. Even in those successful, this peculiar depression and anæmia would continue.

In every case, regardless of the time or length of infection, this clinical picture was always present.

From their history supported by observation, the return of the chills was not as periodic and regular as in the ordinary forms of malaria, and very often the chills would be absent, supplanted by a severe headache and other symptoms of toxæmia.

From a study of the fever charts from these cases, very interesting and instructive data was obtained, for, from Cases III, IV, VI, VII, X, XII, XVI, XVIII, XX, all of which showed æstivoautumnal parasites in their blood; two (namely Cases III and IV) were distinctly remittant, whilst seven (namely Cases VI, VII, X, XII, XVI, XVIII, XX) were intermittent in character; showing conclusively that the æstivoautumnal parasite does not always produce a remittent type of fever. We also find that Cases IV, XII, XV, XVI, XX, represent the quotidian type, whilst Cases III, VI, VII, X, the tertian, and Case XVIII whilst the chart promised a tertian course, terminated as a quotidian.

A study of the fever charts from Cases II, IX, XIV, XIX, all having tertian parasites in their blood, showed nothing, but a typical intermittent course, one however, viz.: Case XIV, was probably a double tertian, as the chart shows us a daily rise. Of the so called mixed infections of tertian and æstivoautumnal or quartan and æstivoautumnal, I have been fortunate to be able to include in this series six undoubted cases.

Cases XI, XIII, XVII, XXIV, XXV, XXVIII, contained tertian and æstivoautumnal parasites. Cases XI, XIII, XXV were distinctly intermittent. Case XVII remittent, and from two Cases, XXIV and XXVIII I was unable to draw definite conclusions.

These features would not seem especially rare in themselves but when supported by a close study of the blood they form a very unique condition.

The blood findings were those of a marked secondary anæmia, associated with leucopenia, and the hæmoglobin ranged from thirty to seventy per cent.

The distinctive white blood count mentioned before is herewith tabulated, as is also the type of parasite found in each case.

	Small lymphocytes.	Large lymphocytes.	Neutrophiles.	Eosinophiles.	Transitionals.	Form of parasite.
Case I—						
“ II—A. T.	41	10	46	1	2	Tertian parasite.
“ III—N. S.	35	10	53	1	1	Æstivoautumnal parasite.
“ IV—W. C.	37	12	51	0	0	Æstivoautumnal parasite.
“ V—						
“ VI—J. E.	48	14	30		8	Æstivoautumnal parasite.
“ VII—F. L.	35	10	55	0	0	Æstivoautumnal parasite.
“ VIII						
“ IX—A. K.	35	8	57	0	0	Tertian parasite.
“ X—H. K.	38	8	52	2	0	Æstivoautumnal parasite.
“ XI—P. O.	44	6	45	4	1	Æstivoautumnal and tertian parasite.
“ XII—J. M.	47	3	40	7	2	Æstivoautumnal and tertian parasite.
“ XIII—H. L.	49	2	47	2	0	Æstivoautumnal and tertian parasite.
“ XIV—L. R.	33	8	59	0	0	Tertian parasite.
“ XV—						
“ XVI—J. J.	31	7	61	1	0	Æstivoautumnal parasite.
“ XVII—W. M.	48	5	45	0	2	Æstivoautumnal and tertian parasite.
“ XVIII—E. T.	35	10	50		5	Æstivoautumnal parasite.
“ XIX—A. M.	41	12	42	2	3	Tertian parasite.
“ XX—E. T.	39	6	51	1	3	Æstivoautumnal parasite.
“ XXI—B. L.	32	10	55	2	1	Tertian parasite.
“ XXII—D. T.	36	18	36	6	4	Æstivoautumnal parasite.
“ XXIII—						
“ XXIV—P. O.	36	14	43	0	7	[1]
“ XXV—A. D.	36	10	50	2	2	[1]
“ XXVI	40	10	43	5	2	Æstivoautumnal parasite.
“ XXVII	54	10	36	0	0	Æstivoautumnal parasite.
“ XXVIII—P. E.	41	12	47	0	0	Æstivoautumnal parasite.
“ XXIX	39	5	56	0	0	Æstivoautumnal parasite.

Summary.

In six cases, the blood of these patients showed the tertian parasite and in same specimen or in subsequent examinations, forms which resembled the æstivoautumnal type.

In five cases. tertian parasite.

In thirteen cases, æstivoautumnal parasite.

AVERAGE DISTINCTIVE WHITE BLOOD COUNT.

	Normal blood count. (Cabot.)	Common malarial count. (De Casto.)	Tropical anæmia. (Talbot.)
Small lymphocytes	20 to 30%	15%	39.5%
Large lymphocytes	4 to 8%	15%	9.2%
Neutrophiles	62 to 70	67%	48
Transitionals	0 - 0	2	1.8
Eosinophiles	½ to 4%	1%	1.5%
Basophiles	1-40 to 9-10	0	.0

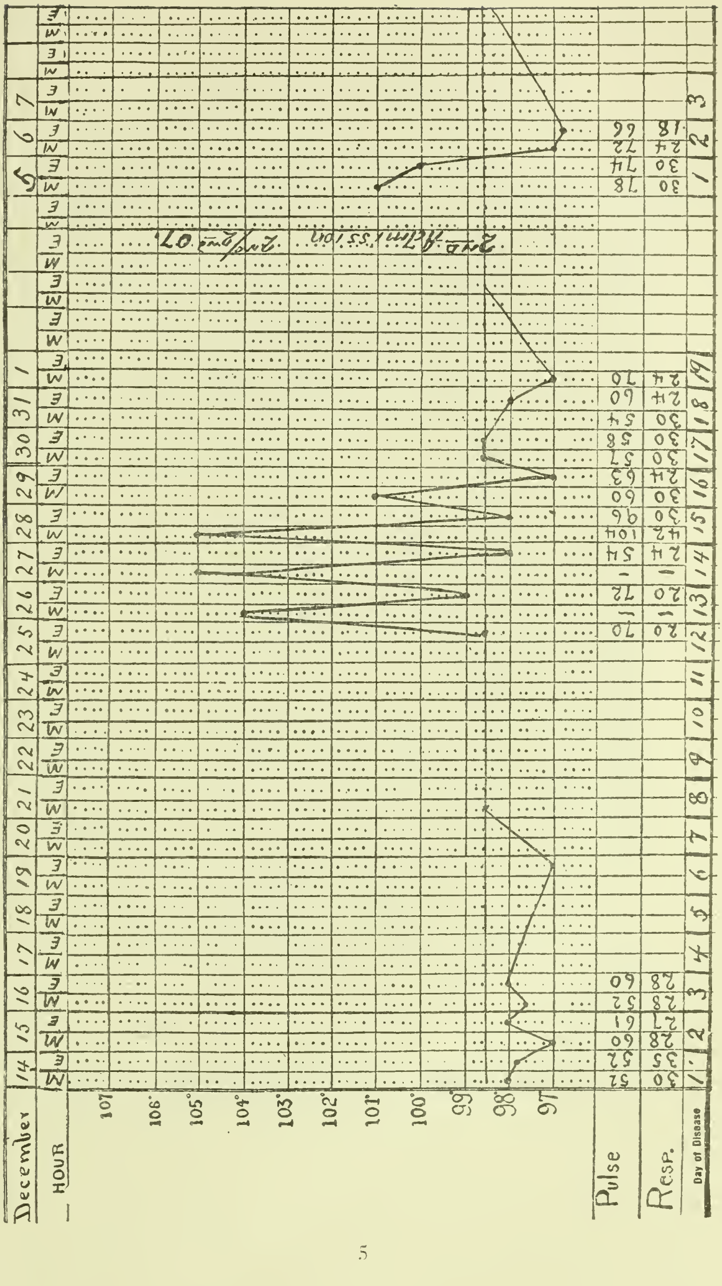

Chart 1.—Case XI.

Synopsis of Cases.

Case II.—A. T., age thirty-five, native of Maryland, laborer, admitted December 4, 1906. Never had any previous malaria, entering Spanish Honduras May 4, 1906, remaining for two weeks, began having chills and fever which continued for six months.

Physical examination: Heart was enlarged, no murmur; liver dullness increased three quarters of an inch in mammary line; spleen was enlarged and easily palpable.

Case III.—M. B., age twenty-four, native of Germany, sailor, admitted November 19, 1906. Never had any previous similar sickness, entering Spanish Honduras October 4, 1906, in two weeks began having chills and fever, sick for four weeks.

Physical examination: Heart, anæmic blow at the apex; liver, not palpable; spleen was enlarged and palpable, very smooth.

Case IV.—W. C., age thirty-nine, native of Ireland, sailor, admitted November 26, 1906, very healthy as a boy and never having chills and fever previously, five days after entering Spanish Honduras received the infection, continuing for two months previous to admission.

Physical examination: Heart, no murmurs audible and not enlarged; liver enlarged and palpable; spleen was enlarged and palpable.

Case VI.—J. E., age twenty-six, native of Honduras, admitted December 4, 1906, healthy up to present illness, had been living in Spanish Honduras for the past five months, during which time he had had chills and fever for which he had taken quinine frequently before admission.

Physical examination: Patient anæmic; heart normal; lungs normal; spleen and liver both enlarged and palpable; urine normal.

RELATIVE WHITE BLOOD COUNT.

	Following quinine.	Before quinine.
Small lymphocytes,	16	48
Large lymphocytes,	15	14
Neutrophiles,	65	30
Eosinophiles,	2	0
Transitionals,	2	8

No ova in stools.

Case VII.—P. L., native of Germany, admitted November 25, 1907, no history of any previous malaria. Some three weeks ago previous to admission while in Central

America, began having chills and fever, the chills occurring every third or fourth day.

Physical examination: Patient anæmic; heart normal; liver not enlarged.

Case IX.—Age thirty-five, native of Germany, admitted December 6, 1906. At twenty-two had chills and fever in the country; healthy as a child. Some nine weeks ago began having chills and fever irregularly in Spanish Honduras. Coming to United States some three weeks ago began having chills and fever every day.

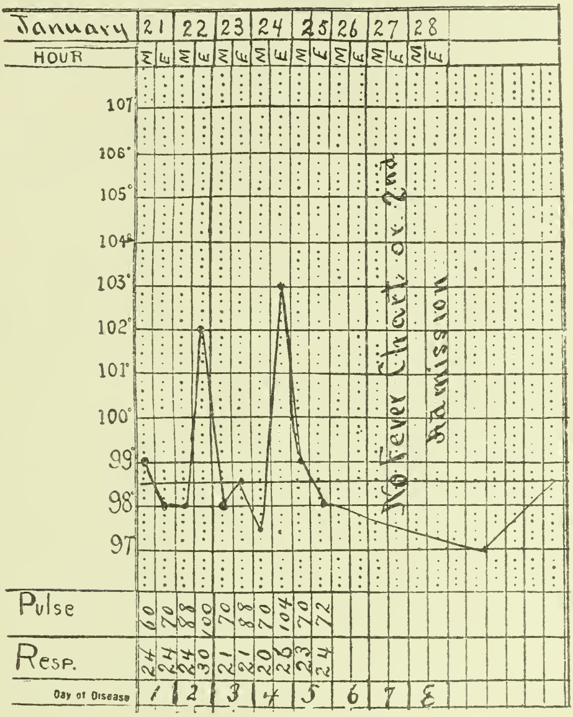

Chart 2.—Case XIII.

Physical examination: Heart normal; patient anæmic; liver and spleen easily palpable and enlarged.

Case X.—H. K., native of Mississippi, admitted December 11, 1906. Patient had never had any previous chills and fever. For past two months had been in Central America, when four weeks previous to admission he began having chills and fever, irregularly at first every day, later every two days.

Physical examination; Patient was anæmic; heart normal, spleen barely palpable, liver same.

Case XI.—P. O., aged twenty-five, native of Ireland, admitted February 2, 1907, healthy young sailor, never had had any previous similar sickness. Entered Spanish Honduras four months ago, one week later he began having chills and fever which continued at irregular periods up to the time of admission.

Physical examination: Anæmic young male; heart enlarged, and palpable, liver negative, urine negative.

Case XII.—J. M., aged twenty-three, native of Canada, admitted January 29, 1907. All diseases common to childhood, alcoholic, no previous similar sickness; some four months ago he entered Spanish Honduras; two months later he began having chills and fever, the paroxysms appearing every other day.

Physical examination: Heart, anæmic blow at the apex, spleen and liver enlarged and palpable; patient very anæmic in appearance; urine showed chronic interstitial nephritis.

Case XIII.—H. L., age thirty-six, native of Canada, admitted January 1, 1907; healthy as a child, never having had malaria before. Some nine months ago he entered Spanish Honduras and one or two months later he began having chills and fever which continued very irregularly.

Physical examination: Patient was anæmic, heart enlarged with anæmic blow at the apex,. liver and spleen enlarged and palpable.

RELATIVE WHITE BLOOD COUNT.

	1-21-07. Following quinine.	3-9-07. Before quinine.	3-11-07. Again after quinine.
Small lymphocytes, ...	18	49	37
Large lymphocytes, ...	13	2	8
Neutrophiles, ...	63	47	55
Eosinophiles, ...	1	2	0
Basophiles, ...	3	0	0
Transitionals, ...	2-100	0-100	0-100
	Tertian parasites.	Aestivoautumnal parasites.	

Case XIV.—L. R., age twenty-one, native of Denmark, admitted April 10, 1907, ordinary diseases of childhood, no malaria, three months ago he entered Panama and some ten days later began having chills and fever, which continued very irregularly.

Physical examination was negative.

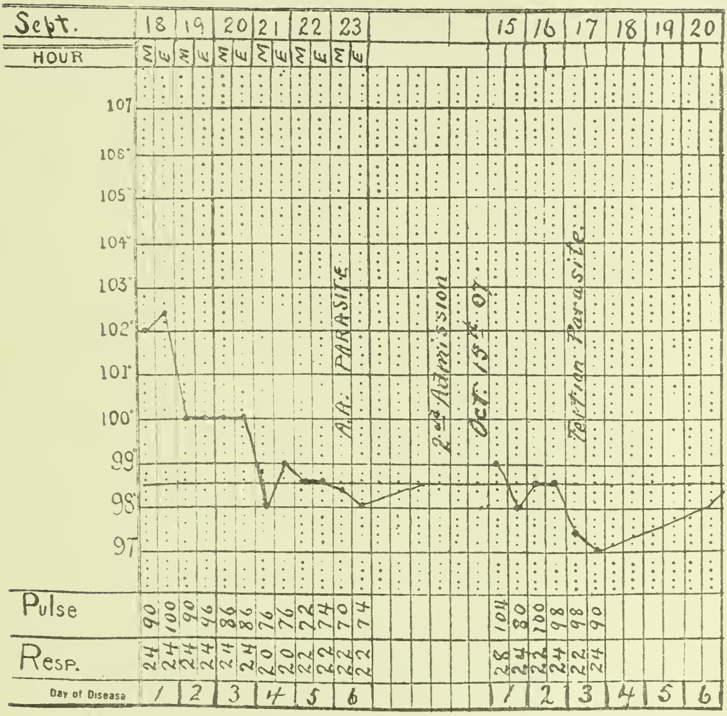

Chart 3.—Case XVII.

Case XVI.—J. J., aged thirty-five, native of England, admitted October 25, 1907. Some three months ago he began having chills and fever in Colon, coming to this country the paroxysms continued.

Physical examination: Patient was anæmic, poorly nourished; skin yellowish; mucous membranes anæmic; heart negative; spleen enlarged; urine negative. Count made following quinine.

Case XVII.—W. M., age thirty-six, native of Ireland, admitted October 25, 1907. Some five weeks previous to admission he began having chills and fever daily in Panama.

Physical examination: An anæmic, well nourished patient; sclera pale and yellow; mucous membrane pale; spleen palpable, one inch below costal border; abdomen tender.

RELATIVE WHITE BLOOD COUNT.

	9/18/07. After quinine.	10/15/07. Before quinine.
Small lymphocytes, ...	22	48
Large lymphocytes, ...	20	5
Neutrophiles, ...	51	45
Transitionals, ...	7-100	2-100
	Æstivoautumnal parasite.	Tertian parasite.

Case XVIII.—E. T., age twenty, native of Italy, admitted October 5, 1907. He had been living at Colon when he was taken sick with chills and fever; no interpreter obtained.

Physical examination: Patient was anæmic; skin yellowish; mucous membrane pale and anæmic; abdomen tender and painful; unable to palpate spleen.

Case XIX.—A. M., age twenty-one, native of Spain, admitted October 18, 1907. Through an interpreter, it was learned that he had been down in Spanish Honduras and there taken with chills and fever.

Physical examination: Patient anæmic, skin and sclera very yellow; spleen enlarged and palpable; urine negative; no ova in stools.

Case XX.—E. F., age eighteen, native of Tennessee, admitted September 13, 1907. Never had had any previous malaria; some months ago while working in Spanish Honduras he began having chills and fever; returning to the States he was well for two weeks when he began having a return of symptoms.

Physical examination: Well nourished young male; heart negative; rest negative.

Case XXI.—H. L., age twenty-one, native of New York, admitted February 16, 1907. Some three years ago had

had malaria, sick for two months. Six months ago he went to Spanish Honduras and after being there for two weeks began having chills and fever.

Physical examination: Young looking male; sclera and conjunctiva pale and anæmic; heart negative; spleen palpable and enlarged; liver enlarged; urine normal.

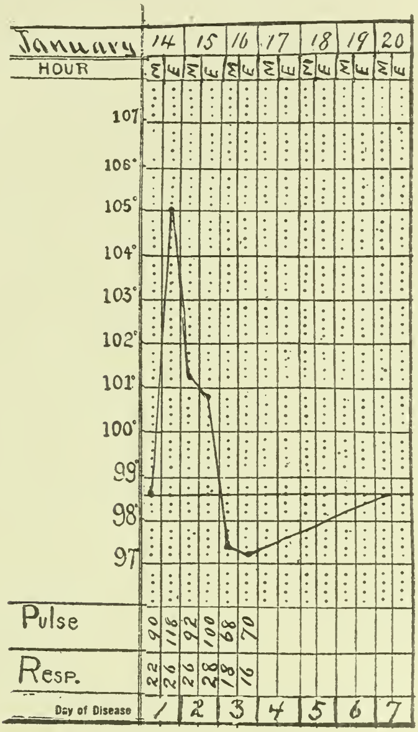

Chart 4.—Case XXIV.

Case XXII.—Dr. T. had been around the coast of Spanish Honduras and southern parts for several years having chills and fever.

Physical examination: Large, healthy looking male; heart normal; liver and spleen palpable; no ova found in stools after repeated examinations.

CASE XXIV.—P. O., age twenty-nine, native of Massachusetts, admitted January 14, 1908, no history of any previous malarial infection. Some two years ago he entered Spanish Honduras and one year and four months later began having chills and fever, which continued very irregularly; when patient came to the States had the chills every day.

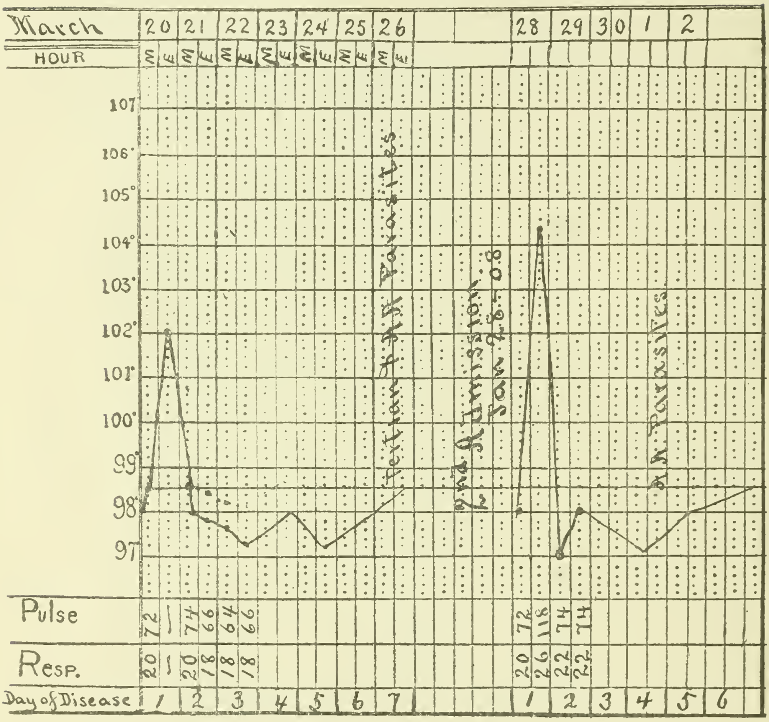

Chart 5.—Case XXVIII.

Physical examination: Anæmic patient: heart normal; liver and spleen both enlarged and palpable; urine normal.

Case XXV.—A. D., age twenty-one, native of Spain, admitted January 18, 1908. She lived in Spanish Honduras for three years when she began having chills and fever associated with loss in flesh and appetite.

Physical examination: Anæmic young female, well nourished; skin doughy and pale; heart enlarged and hæmic murmur at apex; liver and spleen enlarged, stools showed uncinariasis and trichocephalus dispar.

Case XXVI.—Received the present infection in Spanish Honduras. Came to the hospital suffering from pains in various joints and back.

Case XXVII.—Concise history lost, some months before admission while down in Spanish Honduras, he began having chills and fever which continued very irregular up to the time of admission.

Case XXVIII.—P. E., age twenty-two, native of Sweden, admitted January 27, 1908. Very healthy as a child, and for the past four years had been a sailor. After living in Spanish Honduras for eight years, some four years ago he began to have chills and fever. First admission to the hospital December 21, 1907, when both æstivoautumnal and tertian parasites were found in his blood.

Physical examination: Anæmic young male; heart normal; spleen and liver enlarged and palpable; urine negative; no ova found in stools.

RELATIVE WHITE BLOOD COUNT.

	11-20-07. 1st day.	2d day.	3d day after quinine.
Small lymphocytes, ...	41	50	37
Large lymphocytes, ...	12	7	16
Neutrophiles, ...	47	33	50
Transitionals, ...	0	3	0
Eosinophiles, ...	0	7	7
Basophiles, ...	0	0	0
	100	100	100

Aestivoautumnal and tertian parasites.

Second admission, January 27, 1908.

Small lymphocytes, ...	41
Large lymphocytes, ...	16
Transitionals, ...	1
Neutrophiles, ...	42

Aestivoautumnal parasite.

Case XXIX.—J. E., Italian, never had any previous malarial infection, being sick with present illness in Spanish Honduras for three months.

Physical examination: Very anæmic patient; liver and spleen only slightly palpable; other examinations negative.

In the study of these cases all the concomitant diseases that were thought to have any influence upon the lymphocytes were shown to be absent. On looking at the counts, we notice at once the relative and constant increase in small lymphocytes ranging from thirty-five to fifty-four per cent. This is the point to which our attention would at once be called and to which I desire to lay especial importance.

In the study and research work done on our blood diseases in this country and lower tropical ones, we have come to depend upon a relative count as of great aid and help in assisting one to diagnosticate various blood diseases, both of primary and secondary origin. In fact, it is of absolute value before we can begin to understand the diseased condition.

Every blood disease has its picture within certain bounds, e. g.; pernicious anæmia, splenomedullary leuchæmia, lymphatic leuchæmia, malarial fever, parasitic diseases, and others. Although the relative leucocytic count has not been studied in every disease we at present must infer that there must be some change in the leucocytes yet, undetermined representing a certain organism or toxine.

The constancy of the relative blood count in any disease must depend upon the liberation of a certain toxine or some other influencing agent upon the blood. The leucocytes respond in a peculiar relation differently for different toxines, being constant for that toxine. If our study continues along proper lines, it seems possible by finding the relative leucocytic count we will be able to recognize different toxines by this relation. In the cycle of reproduction of organisms, which are supposed to be producing a certain train of symptoms in a patient, toxines are liberated which are peculiar to that organism alone. As every organism breeds true to themselves, the same toxine is constantly being liberated. This causes a reaction upon the constituents of the blood manifested mostly upon the leucocytes, the relation of which should be constant for every different toxine or disease when uninfluenced.

In the ordinary forms of malaria present in this section and in the tropical region where the common organisms (tertian, æstivoautumnal, and quartan) are found, we find in the relative leucocytic count a very valuable aid in their diagnosis. We find the most prominent writers on this subject to agree with the conclusion and depend upon it for diagnostic value in malaria, that there is a relative increase of lymphocytes, mostly evidenced in the large lymphocytes. When we find this relation existing and being unable to find the parasite in a case presenting malarial symptoms we treat it as such with the best of results.

These cases which I have collected, however, present a different feature in their leucocytic relation.

While as a rule I have found an increase of lymphocytes, the increase is shown in the small, rather than the large varieties. In addition to this the parasites found have been of a very erratic form, at times presenting outlines of a tertian then again of an æstivoautumnal parasite in the slide of blood and in the same patient's blood at different periods of the illness as shown in the charts. How are we to interpret such a phenomenon, a blood picture which was constant in a series of twenty-four cases as presented? Shall we designate it along with the ordinary forms of malaria or shall we infer that we are dealing with a different toxine produced by a different parasite? This last conclusion seems to me the most plausible, for after a careful study of the blood the history and clinical symptoms of the cases we must infer that a very strong chain of evidence is thus produced. If we infer that these classes of cases represent a type of the æstivoautumnal malaria then the usual distinctive leucocytic count (relative large lymphocytosis) used as an aid in the diagnosis of malaria would not hold true in the hæmatology of malaria. The blood of these patients is continued to be studied, and, while as yet I have found no definite and constant cause for the condition, the results obtained so far have been very favorable.

In presenting my paper I am greatly indebted to our retired professor of medicine, Dr. J. B. Elliott, for his untiring aid and ready suggestions in the work without which I would have been considerably handicapped.

709 Maison Blanche Building.

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SOME ANALOGIES BETWEEN MALARIA AND SYPHILIS.*

BY WILLIAM H. DEADERICK, M.D., MARIANNA, ARK.

MALARIA has many points of similarity with Texas fever and kala-azar. Syphilis is closely allied to tuberculosis, leprosy and the eruptive fevers. But for striking analogies with reference to clinical course and to treatment, malaria and syphilis are probably more closely related than any other two diseases.

Both are notoriously protean in nature and are manifested by an infinite variety of expressions. Malaria with her mildest chill, deadliest blackwater fever, cachexia, masked forms and pernicious paroxysms, and syphilis attacking every tissue in the body, from top to toe, from skin to bone, are probably unparalleled for diversity of aspect.

Both diseases, to be acquired, must be innoculated.

Both have stages of latency during which there are no symptoms and the patient is apparently cured. Malaria may lie entirely dormant for many months after the last possibility of infection, and then become sufficiently aroused to prove fatal. For example, the cases of pernicious malaria that occur months after leaving the focus of infection. So, also, does syphilis behave and may surprise the patient years after infection or may even appear in the children of a parent believed to be long free from the disease.

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* Read by title at the sixth annual meeting of the American Society of Tropical Medicine, held at the United States Naval Medical School, Washington, D. C., April 10, 1909.

The pathognomonic evidence of malaria, the deposition of melanin in the viscera, may aptly be likened to the characteristic process of syphilis, the formation of the gumma.

In the field of therapy, malaria and syphilis present almost perfect parities.

The only two diseases for which we possess almost true specifics are malaria and syphilis.

The specific effect of drugs is, however, correspondingly limited in the two diseases. In syphilis, appropriate medication causes the rapid dissolution of the visceral gumma, but is impotent against the resulting cicatrix which may prove fatal. In pernicious malaria characterized by localizations of parasites, while quinine may promptly kill the organisms, it avails nothing toward the amelioration of perivascular exudation, hemorrhage or necrosis depending on parasitic occlusions.

Following both diseases are "para-affections," in the treatment of which the respective specifics are relatively useless. Such are hemoglobinuric fever and certain forms of splenomegaly after malaria, and tabes and general paresis following syphilis.

The too early application of the specifics has the same disastrous effect on the diagnosis in both cases. After the administration of quinine in malaria, it is almost, if not quite, impossible to find the parasites, and the temperature curve is thereby so distorted as to be valueless. The effects of anti-syphilitic treatment on the induration and other diagnostic criteria in syphilis is too well known to call for comment.

The happy effect of mercury and the iodides in syphilis rendered, for a long period, very uncertain the length of time necessary to continue the treatment. This was learned only by experience and at the expense of lives, and is usually fixed, more or less arbitrarily, at two or three years. At the present day, physicians no longer mistake the complete disappearance of syphilitic symptoms for a cure, but continue the treatment daily during the first months, then interruptedly, commonly during alternating months. But not so with malaria. As soon as the temperature is normal, and even before the blood destruction is compensated, the specific is often discontinued, to be resumed only when relapses occur, which is the rule. A few days' treatment with quinine no more cures malaria than does a few weeks' rubbing with mercury cure syphilis. This abortive quinine treatment may destroy the asexual forms of the parasites, but the parthenogenetic forms, by a sort of immaculate conception, have the faculty of tiding the generation over the catastrophe and occasioning a fresh outbreak or maintaining latency for months or even years.

The danger to the community arises from the latent stage in each disease. The syphilitic, with enlarged lymphatics, syphilides or other evidence of disease is shunned, and from mortification, if from no other motive, will take treatment, but the victim of latent syphilis may infect a score of people.

The subject of active malaria usually seeks treatment of some sort. He often feels too bad to move in public, and the duration of the active stage is short. With latent malaria, however, the patient believes himself cured, is able to follow his occupation, takes no specific and may be a fountain of infection for an indefinite time.

For these reasons the chief obstacle to the eradication of syphilis from society is the subject of latent syphilis; the reason for the failure in permanent results of the Koch method of the prophylaxis of malaria is the detection and control of the subject of latent malaria.

THE RELATION OF HOUSE-FLIES TO THE SPREAD OF DISEASE

By HENRY SKINNER, M. D., President of the Entomological Society of America, Philadelphia.

The house-fly, *Musca domestica,* was described by Carl von Linne in 1758. It comes in the order *Diptera* (or two-winged flies, and belongs in the family Muscidæ. The transformations are complete, there being four stages—the eggs, the larvæ and the puparium (containing the chrysalis) and the imago or perfect insect.

The egg is white, elongate, oval, cylindrical, a little smaller and more pointed at the anterior end than the posterior. Its length is .04—.05 of an inch and about .01 inch in diameter. In shape it is more or less like a slender grain of wheat and has a groove on the side. The eggs are usually deposited by the female in warm and moist horse-manure in masses in the crevices. Heat and moisture are required for their normal development, and they hatch in about twenty-four hours after oviposition. The freshly-hatched larvæe or maggots are .07 inch in length, tapering at or pointed at the head end and blunt at the other. When fully grown they are from .25 to .40 inch in length. They moult or change their skins three times, and the entire life of the larvæ is from five to seven days. After the third molt it changes to an inactive or resting stage, the pupa or puparium. This is a small, elongate brown, segmented object, rounded at the ends and contains the chrysalis. This latter stage lasts from five to seven days, when the imago appears. Thus, the whole life cycle is about fifteen days.

The body of Musca domestica is black; the head has a longitudinal reddish, oval, smooth area on the vertex, with the orbits and adjacent region golden or silvery in some lights; the hairs are black and the antennæ and plume black. The thorax is black, tinged with golden rays on the sides, with three dorsal gray longitudinal bands, the middle one most distinct, the two lateral ones partially interrupted in the middle and continued onto the scutellum; there is a broad lateral golden gray band interrupted by the sutures. The base of the first abdominal segment has a yellowish band interrupted in the middle. On the middle of the end of the two succeeding segments is a triangular mesial golden spot, with an irregular band on each side, and farther down the sides golden; terminal segment, golden. Base of wings, scales and halteres, yellowish white. Legs black. The male differs from the female in the front between the eyes, being about one-third as wide as in the latter, while she is rather the smaller. Length, .22 to .32 inch.

The tongue is comparatively short, fleshy and bilobed and blunt, incapable of biting or piercing the human skin, and is adapted only for lapping up liquids. Allied species which bite may be confused with the house-fly.

The legs are very hairy and the fly, in walking on rough surfaces, uses the tarsal claws, and, on smooth surfaces, a fleshy organ called the pulvillus, which secretes a fluid that enables the fly to hold on to glass or like surface.

This insect will oviposit in horse-manure, decayed vegetables, decayed meats, cow-dung, fowls' dung and human excrement. The vast majority of them are, however, bred in horse excrement. Further knowledge in regard to the food of the larva is desirable. It would be useful to know about what proportion breed in garbage and in decayed meats, as this is important from a medical standpoint when preventive measures are considered.

Historical.—The house-fly has long been considered a nuisance, but it was held at one time that they were beneficial insects, owing to the habits of the larvæ in the destruction of effete substances. One writer, in 1890, says, in regard to the destruction of house-flies, "that if such an attempt were both practicable in operation and profitable as to numbers produced, it would still be unadvisable from a sanitary point of view, the annihilation of every house-fly would breed a pestilence." It is thought by many persons, including physicians and entomologists, that the relationship of insects to the dissemination of disease is a new idea, but the facts are quite the contrary, as a brief review will show.

Sydenham (1624-89) held that if house-flies were abundant in the summer, the autumn would be unhealthy. Holscher (1843) took the contrary view. Crawford (1808) believed that insects were instrumental in carrying disease. The literature is replete with instances of the transferring of diseases by insects other than house-flies, but they need not be considered here. Leidy, in 1873, published an article on the pestiferous house-fly, and in 1871 stated that he believed house-flies were responsible for the spread of hospital gangrene during the Civil War.

Sir John Lubbock (1871) also calls attention to the fact that flies alight on decomposing matter and carry that which is impure and unwholesome, notably the secretions of unhealthy wounds, and further says: "Far from looking upon them as dipterous angels dancing attendance on Hygeia, regard them rather in the light of winged sponges spreading hither and thither to carry out the foul behests of Contagion."

By reference to the accompanying bibliography, other references of an early date may be found. C. V. Riley, in 1887, in a general article on insects, speaks of the propensity of the house-fly to carry disease. Celli (1888) fed flies with cultures of the Bacillus typhi abdominalis and proved that the bacilli in the dejecta of the fly were virulent. In 1889 Dr. R. H. Lamborn offered three prizes of money for the best essays for observations and experiments upon various insects that destroy mosquitoes and house-flies, stating method of and capacity of destruction. This stimulated a great interest in that subject among entomologists, and the published results were valuable in many ways.

In 1899 the writer published a brief article calling attention to the danger from the house-fly as a carrier of typhoid fever. The communication was made at a meeting of the Entomological Section of the Academy of Natural Sciences of Philadelphia. The Rev. Henry C. McCook, D. D., who was present, stated that he had visited all the principal camps in the United States and Cuba during the war with Spain, and that house-flies swarmed in the mess tents, and that in many of the hospitals the mouths of the sick soldiers were covered with these disgusting insects. About this time it was held by some that house-flies could not carry typhoid fever, because they did not breed in human excrement. This led Howard to investigate the subject, and he published his paper (1900) entitled "A Contribution to the Study of the Insect Fauna of Human Excrement."

Dr. Victor C. Vaughan, in 1900, read an important paper on the activity of flies in the dissemination of typhoid fever. In 1898, also, treated of the same subject, especially in regard to spreading the disease in camps. The importance of the subject was gradually being recognized and appreciated, and renewed attention was given to it (1904) through the report of the Commission appointed by the Government to investigate and report on the origin and spread of typhoid fever in the United States military camps during the Spanish War of 1898.

In 1902 Howard published an important paper on "How Insects Affect Health in the Rural Districts." In the last few years the literature has grown to considerable proportions, and its interest and importance are being generally recognized by the medical sanitation and medical biologist. Health boards and other civic bodies are also giving the subject thought and attention. It is to be hoped that in the future the frightful mortality that occurs from this cause in war will be avoided. Few seem to know to what a great extent war is dependent on a knowledge of bacteriology and entomology.

The knowledge of bacteriology, in conjunction with a knowledge of the habits of the house-fly, its settling on all kinds of food, in addition to its habit of alighting on all sorts of effete germ-laden material, show conclusively that it is a very dangerous insect, so far as the health of mankind is concerned. Its hairy body, legs and feet, in conjunction with the spongy pulvillus, make it an ideal carrier of bacteria. That it is a good destroyer of decomposing and fermenting animal and vegetable matter is also true, but it is so dangerous in other ways that it is incumbent upon humanity to take care of and do away with effete material. If this is done, the fly ceases to be necessary as a scavenger. An epidemic of typhoid fever is not infrequently started by the breaking of a small sewer, emptying into a large volume of creek or river water. How much greater is the danger when swarms of flies settle on typhoidal stools and fly to and alight on food? In the latter case there is a virulent and direct transmission to the alimentary canal of the victim. In some instances at Chickamauga it was necessary to walk through human excrement to get to the latrines. In army camps, to deposit human excrement outside of the appointed place is a crime equal to murder. House-flies swarmed there, and if typhoid fever had not existed it would have been a miracle. During the Spanish War a portion of the Second Regiment, Pennsylvania Volunteers, was quartered on the Brandywine Creek, in Pennsylvania, and the surgeon directed the men to use as a sink an abandoned and bottomless canal boat, in the Delaware River, and not a single case of intestinal disease occurred. This was not an ideal method, but it shows results in the way of contrast.

A source of danger that has probably been overlooked is that arising from the fact that feces often containing the Bacillus typhosus is distributed along the tracks from railway trains. House-flies could very readily contaminate food from this source in the homes of persons living along the railroad. About ten years ago there was an interesting law-suit in Philadelphia, probably the first of its kind in the world. Mr. Gabriel Upton sued the city for damages on account of having contracted typhoid fever. A verdict of fifteen hundred dollars was awarded the plaintiff. The case was won largely on account of the great probability that the fever was carried to the individual by *Musca domestica*. The city diverted a sewer into a natural stream that ran by Upton's house and alongside his dining-room. Cases of typhoid fever were proven to exist on the line of the sewer. A large amount of fecal matter came down the stream, and at times it was necessary to start it going when the water was low. The case was appealed by the city to the Supreme Court of Pennsylvania, but the city settled for the full award of the jury.*

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*Gabriel Upton vs. The City of Philadelphia. Court of Common Pleas No. 4. March term, 1897. Appealed to Supreme Court of Pennsylvania Jan. term, 1899.

It is hardly necessary to dwell longer on this subject of typhoid fever, as the possibilities of the case are so self-evident. Wherever flies can gain access to material containing the *Bacillus typhosus* they are almost certain to carry it to food.

House-flies have long been suspected of being agents in the dissemination of cholera, and a number of articles have appeared on the subject since 1853. That they contaminate the food of the well from the vomit or dejecta of those ill from the disease, in times of epidemics, is undeniable. The worst cholera months are said to be those in which these insects are most abundant. Nuttall says: "The body of evidence here presented as to the rôle of flies in the diffusion of cholera is, I believe, absolutely convincing." It is also known to carry other intestinal diseases. So far as known, the house-fly is only a mechanical conveyor of bacteria, and is not the host of any known animal disease producing organisms similar to the protozoan organisms that cause malaria, and of which the mosquito is the agent of dissemination.

Those who practiced medicine some years ago will recall the condition of the sick-room of the patient ill with tuberculosis, where some kind of open receptacle was used in which to expectorate, and said receptacle and the surrounding floor covered with house-flies, either feeding or wading. As they are somewhat omniverous and like change of diet, they next reported to the dining-room, in the same house or next door. It was also no unusual thing to see them feeding from the lips of the patient, who did not have enough energy left to drive them away. A number of observers have shown that ingested sputum discloses virulent tubercle bacilli in fly-specks (excrement), and that the bacilli may remain virulent for several weeks. Pus from discharging sinuses and fecal matter from tuberculous patients are also sources of danger in this respect. Various kinds of food-stuffs exposed on the street for sale are potent sources of danger, and liable to contamination by flies which have walked or fed on the sputum expectorated on the sidewalk. Feather dusters are used by the vendors of fruit to brush off the larger part of the day's accumulation of street dirt, dried sputum, fly excrement and dessicated horse-manure. What the brush misses the purchaser eats.

Some of the well-known remedies need only be mentioned briefly, as, sooner or later, preventive measures will come to the fore. Wire screeens, sticky papers, poison papers, wire traps, fumigation with pyrethrum powder, etc., all have a limited use. It costs anywhere from ten cents to five hundred dollars to screen a house, and it hardly seems fair that stable-owners should impose this tax on their neighbors. Moreover, it might be proper to ask them to pay physicians' fees, nurses' and druggists' bills where sickness is caused by neglected stables.

The keynote to the situation is along the line of prevention. Horse-manure bears about the same relation to the house-fly that stagnant water does to the mosquito. If this insect is prevented from ovipositing in manure, the fly as a pest would be largely a thing of the past. Various substances have been mixed with manure to destroy the fly larvæ, such as kerosene, chloride of lime, "residual oil," lime and phosphates. These have been used with more or less success. Stables should have smooth and hard floors and kept clean, so that manure cannot accumulate. It should either be used at frequent intervals or stored in properly constructed bins or screened apartments. A good method is to ram it tightly in barrels that can be tightly covered. The most economical way of caring for very large quantities has not been determined. In towns and villages it would probably pay to have it collected at stated intervals, as is the case with garbage and ashes. The automobile may become a factor in the destruction of house-flies, as in the near future the horse may have only a limited use. The problem is a very simple one, and as soon as preventive measures are inaugurated more extensively the effective and economical measures will be discovered.

A distinguishd surgeon recently wrote me in regard to this subject as follows: "The matter is one of great interest to me, as indeed is the whole question of the prevention of the multiplication of flies, as a matter in which applied science has made but little progress. The person who discovers a cheap and effective way of destroying flies in and around a given locality will, in my opinion, be one of the great practical benefactors of the race. He would be as sure of immortality as Lister." If the people went to half the trouble to prevent flies that the surgeon takes to bring about asepsis or antisepsis, the object would be accomplished.

The house-fly problem at the present time involves the awakening of the people to the exigencies of the case, and the necessity of preventive measures and the expense necessary would be justified by the result. The house-fly is distributed practically all over the world, and in tropical and semi-tropical countries it is more numerous and a worse pest than it is in the temperate zones.

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Discussion.

Dr. P. M. Ashburn, of the United States Army, said that a year or two ago he had had a number of slides covered with yaws serum, when he discovered a busy fly engaged in eating some of the serum. He caught the fly, and found in its proboscis two larval nematodes that were indistinguishable from strongyloides. He thought that in this way the fly might be a bearer of intestinal parasites—possibly of uncinaria. Dr. Skinner had mentioned the greater prevalence of flies in the tropics, but Dr. Ashburn said that from personal observation of conditions in the Philippines he would state that house flies were much less common there than in the United States in the summer time. He had recently been making inquiries in regard to their prevalence in Liberia, and had learned from a gentleman who had spent a good deal of time in that country that the house fly was very uncommon there as compared with this country.

Dr. O. T. Logan, of Changteh, China, said that in China the blue bottle fly was more common than the house fly.

Dr. W. P. Chamberlain, of Jackson Barracks, La., confirmed Dr. Ashburn's statement that house flies were less common in the Philippines than in the temperate portions of the United States in summer.

Dr. George Dock, of New Orleans, said that the only way to get rid of house flies was to observe absolute cleanliness. For the benefit of those living near stables, he mentioned a method of keeping flies down that he thought pretty effective. It was first

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mentioned in a French medical journal about a year ago, and attention was called to it by Dr. W. S. Carter, of Galveston, who kept his laboratory free from flies by having soup plates containing sugar water and formalin placed about the room. It was only a one per cent. formalin solution. Dr. Dock repeated this experiment, but was not so successful, and found that this was because the solution used was not strong enough. In reading over the French article, he discovered that a ten per cent. solution had been used. The odor could not be perceived, but the flies were absolutely destroyed. The plates became filled with them, but none were seen around the room.

Dr. H. L. VIERECK, of Washington, said that at a laboratory in Harrisburg, Va., while specimens were being immersed in four per cent. formalin, it was found that flies were attracted by the formalin solution, which they lapped up, and from which they died in great numbers.

Dr. SKINNER said that there were numerous records of places in the tropics in which house flies were very abundant. He considered that it would be very valuable to get further information in regard to the distribution of the house fly. It was distributed pretty well all over the world, and, from accounts in various journals, seemed to be especially prevalent in southern Europe. He thought that it would be of great interest if some of the gentlemen who had absolute knowledge of its distribution in the tropics would publish this information. He himself would be glad to obtain such articles and have them published. The distribution of all objects in nature was of great interest, and everybody would be glad to learn why flies were scarce or did not exist in some places, as this might be the means of bringing out important scientific facts.

UPON THE MECHANISM OF THE NEUTRALIZATION OF COBRA VENOM BY ITS ANTITOXIN.*

A. CALMETTE,
LILLE, FRANCE.

On account of their resistance to heat and on account of the property which they possess of not being modified by different reagents, such as weak acids and alcohol, certain venoms lend themselves to the chemical and physiological study of their combinations with antitoxins better than microbic toxins.

In 1895 [1] I showed that if definite proportions of venom and antivenomous serum are mixed in vitro and then heated at 67° C for one-half hour, the injection of the heated mixture killed the animal as if it had been inoculated with the venom only. One might conclude from this that antitoxic serum did not destroy the toxin with which it was mixed, and that if a chemical combination was formed between the toxin and the antitoxin, that combination was resolvable into its elements, which remained intact side by side.

C. J. Martin and Cherry,[2] in repeating these experiments, found that they were quite exact when the mixture of venom + antitoxin was heated within ten minutes after it had been made, but that if it was not heated until twenty or thirty minutes later, the toxicity of the venom would not reappear.

J. Morgenroth [3] then showed that when a small quantity of hydrochloric acid was added to the atoxic compound of venom + antitoxin and the mixture heated at 100° C. for thirty minutes, the mixture was able to restore the half of its neurotoxin.

In some recent experiments made in collaboration with L. Massol, I have tried to determine the precise action of heating in the dissociation of neutral mixtures of venom and

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antitoxin. I have shown, first of all, that antitoxin alone is normally destroyed by any temperature above 68° C., if it be continued for ten minutes. But when antitoxin is mixed with the venom it acquires a marked resistance to heat. The dissociation is produced only when the temperature reaches 75° C. Then the mixture again becomes toxic.

If the mixture is acidulated beforehand with a little hydrochloric acid (.6 cubic centimeter normal hydrochloric acid for one cubic centimeter of a .5 per cent solution of venom) and then heated, the dissociation will be effected at 72° C. and the restitution of the venom will be complete. Hydrochloric acid, therefore, restores the thermolabile property to the antitoxin, and the mixture of venom + antitoxin becomes dissociable at a lower temperature.

Other experiments have shown this same dissociation by another method, based on the curious property which alcohol possesses (fifty to eighty per cent) of dissolving the toxic substance of cobra venom, but not the antitoxin. If .1 cubic centimeter normal hydrochloric acid is added to each cubic centimeter of serum and a convenient quantity of alcohol is added to a neutral mixture of venom + antitoxin, the freed venom will immediately dissolve in the alcohol, whilst the precipitated antitoxin will become inactive. The following is the method of the operation:

To ten cubic centimeters of a neutral mixture of serum + venom, containing ten milligrams of venom, 1.5 cubic centimeters of normal solution of hydrochloric acid are added and a sufficient quantity of alcohol to make the total volume one hundred cubic centimeters and a dilution of 72° C. (Gay-Lussac). After centrifugalization the precipitate is washed once with alcohol at 50° C. (Gay-Lussac). The precipitate remains in contact with the alcohol for fifteen minutes. The precipitate and the liquid are then collected separately in four hundred cubic centimeters of water. Each is partially neutralized. Each of the two portions is evaporated to twenty-five cubic centimeters. One-half cubic centimeter of the liquid, corresponding to two hundred milligrams of venom, injected into a mouse will kill in one hour. The precipitate, on the other hand, is antitoxic and is again rendered thermolabile.

In another series of studies relative to the precipitating action of the antivenomous serum in relation to cobra venom I have been able to convince myself that when the venom is exactly neutralized, it always forms a precipitate in the mixture. This atoxic precipitate may be separated by prolonged centrifugalization. Upon drying, it becomes insoluble in slightly acidulated physiological salt solution; but if the salt solution is added while the precipitate is fresh it will redissolve very easily. The insoluble dry precipitate may be put in fine suspension in water and artificially digested either with trypsin or with Merck's papain. It is easy to show that the digestion (tryptic particularly) destroys a part of the antitoxin fixed upon the venom and liberates a small portion of the latter. In slightly acidulating the mixture after digestion and heating it to 72° C. for one hour, the venom is entirely recuperated and again becomes capable of combining with a new quantity of antitoxin.

These facts show that, as I have proved in 1895, at least so far as venoms are concerned, the mixtures of venom and antitoxin form merely an unstable chemical combination. I have been able to dissociate some of these mixtures more than two months after they have been made. It is necessary, then, to admit that the toxin and the antitoxin adapt themselves to each other as a key to a lock; but each of the two substances preserves its individuality in the mixture, and separation may always be accomplished.

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The Journal of Medical Research, Vol. XXI., No. 1, July, 1909.

Extracted from the American Journal of the Medical Sciences, September, 1909

THE VARIOUS TYPES OF PLAGUE AND THEIR CLINICAL MANIFESTATIONS.[1]

By Khan Bahadur N. H. Choksy, M.D.,

SPECIAL ASSISTANT HEALTH OFFICER TO THE BOMBAY MUNICIPALITY, IN CHARGE OF THE ARTHUR ROAD INFECTIOUS DISEASE HOSPITAL AND THE MARATHA PLAGUE HOSPITAL, BOMBAY, INDIA.

The invasion of the human organism by Bacillus pestis manifests itself in certain well-defined and clinically recognizable forms. Their development is determined solely by the path of entrance of the virus into the system: (*a*) If the infection takes place through the skin, by the bite of a rat-flea, or any other agency, and is conveyed into the lymph glands by the lymph stream, the *bubonic* type is the result; (*b*) if, under identical conditions, the infection becomes localized in the skin and subcutaneous cellular tissue, with or without secondary involvement of the lymph glands, the *cellulocutaneous* type ensues; (*c*) if, again under the same circumstances, the blood stream becomes directly infected, the *septicemic* type develops; and (*d*) if the lung-tissue becomes primarily infected, through inhalation or other causes via the air passages, the *pneumonic* type ensues.

Four clinical types are, thus, capable of differentiation at the bedside, each having special characteristics of its own, and each with an important bearing upon the prognosis. The almost classical and synonymous association of the word buboes—*emerods* in Biblical language—with plague, absorbed the whole attention of the observers to the exclusion of the other types, when the disease first broke out at Bombay. Clinical observation, however, soon revealed the presence, as Childe[2] was able to demonstrate, of a few cases of the pneumonic type in 1897. Subsequently the septicemic type was encountered and described by several observers, including myself; and finally, after careful study of a number of cases, extending over three epidemics, I was enabled to verify and describe the cellulocutaneous type in 1900.[3]

All these types do not prevail to the same extent. Hospital experience at the Arthur Road and Maratha Hospitals at Bombay,[4] throughout twelve epidemics comprising over 13,600 cases, shows that the *bubonic* type contributes 92.8 per cent. of all cases; the *cellulocutaneous* type, 3.7 per cent.; the *septicemic* type, 2.4 per cent.; the *pneumonic* type[5] 1.0 per cent.; and *pestis ambulans,* 0.1 per cent. These ratios, however, are not constant even for all of India; and in other parts of the world many variations have been recorded. At Hongkong, for instance, Koch[6] has reported the following incidence: The bubonic type, 63.6 per cent.; the septicemic type, 31.4 per cent.; and the pneumonic type, 5 per cent., in 510 patients observed during 1904.

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[1] Read by title at the sixth annual meeting of the American Society of Tropical Medicine, Washington, D. C., April 10, 1909.

[2] Transactions of the Medical and Physical Society of Bombay, 1897.

[3] Some Observations on Plague and its Treatment with Lustig's Serum, Transactions of the Medical and Physical Society of Bombay, 1900.

[4] N. H. Choksy. An address on the General Pathology and Serum Treatment of Plague, 1908.

I. THE BUBONIC TYPE. Within three days after infection and usually without any prodromes,[7] the patient becomes suddenly ill, sometimes in the midst of his work, has a rigor, feels giddy, and may even fall in the act of walking. The temperature begins to rise almost immediately and simultaneously with it, pain and tenderness in the infected glands are complained of. Such glands may be situated in different parts of the body, the order of frequency being the femoral, inguinal, and iliac glands, separately but more often in continuation, the axillary, and the brachial chain with the epitrochlear, the cervical, parotid, and submaxillary glands, and but rarely those in other positions, such as the femoral chain, the popliteal, in the calf, at the ankle, at the bend of the elbow, pre-auricular, or even occipital. The eyes become suffused, the mind somewhat dull, the speech faltering, and the expression either apathetic or anxious and frightened The patient is generally averse to acknowledge that he is at all ill, and often refuses to take to his bed. Even if convinced that he is afflicted with plague—for there exist but few who do not realize it—he persists in ascribing his symptoms to a chill or exposure, and the swelling and pain in the bubo to a sudden strain and more often to the initial fall. On the other hand, it often happens that the patient not only apparently deludes himself, but succeeds in deceiving those around him, by denying the presence of pain or tenderness in the bubo, and if the medical attendant is not confident or resolute in his diagnosis, he shares the same fate, to the ultimate ruin of the patient. As the temperature rises, the pulse becomes quickened, usually out of all proportion to the normal ratio, is found to be of low tension and easily compressible, even within a few hours. There may be nausea or vomiting, mostly of bile, and by the evening the temperature becomes elevated to 104° to 105°; there is restlessness and insomnia, if not actual delirium. Pain and swelling in the bubo are more noticeable, and periglandular œdema may appear. The patient thus presents within a few hours all the cardinal symptoms of plague.

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[5] Major G. Lamb, I.M.S. The Etiology and Epidemiology of Plague: A Summary of the Work of the Plague Commission, 1908. The Plague Research Commission states that the proportion is about 2.5 per cent., and that is probably correct, inasmuch as many cases go unrecognized and others succumb at home.

[6] Colonial Medical Report for Hong Kong for the Year 1904, Journal of Tropical Medicine, August 1, 1905.

[7] No local lesion is noticeable at the seat of infection except among 8 to 10 per cent. of cases.

The following morning a slight remission in the temperature may or may not be observed, but without any amelioration; all the symptoms, general and local, become more intensified; the tongue is now dry and presents the characteristic appearance of wash leather, but with a red tip and margins; the weakness of the circulation is more pronounced, and the extremities are cold. The patient does not like to be disturbed out of the position he may have assumed, resents all or any interference, is obstinate, and refuses nourishment and medicines; there is extreme irritability, coupled with greater dulness of the mental faculties; the speech is thicker, the syllables being drawn out, or there may be aphasia; delirium may exist; and the temperature rises to the same or even a higher range than the first day. After a restless night and the lapse of forty-eight hours, there appears a distinct and perceptible remission in the temperature, varying from 1° to 4° or more, with or without apparent amelioration. If the former, it is extremely deceptive and of short duration, inasmuch as within a few hours there is a complete change for the worse in every respect. The usual course however, is for the remission to be unaccompanied by any temporary improvement. As all the symptoms become more and more aggravated, the buboes are larger and more prominent, the local œdema greatly increased, the pulse feebler. By evening the temperature again becomes elevated to the same or even a higher level than on the previous days. With these symptoms the patient may be said to enter the most critical phase of the disease, inasmuch as the following two days decide his fate—the average duration of fatal cases being but five and one-half days. Here we are practically at the parting of the ways the future depending upon two factors: (1) It depends upon the extent of the cardiovascular paresis, as also upon the acute infective degeneration of the myocardium brought about by the toxemia. These lead to sudden cardiac syncope or gradual enfeeblement of the circulation, with eventual heart failure, preceded by a slowly progressive œdema of the lungs, owing to the vicious circle set up between the circulatory and the respiratory apparatus. Should this occur, death usually takes place between the third and fifth days of illness. Fully 82 per cent. of all deaths among these cases occur within this period, and 18 per cent. thereafter. The average rate of recovery among them is about 55 per cent. (2) It depends upon the presence of septicemia, for it is about this period, that is, the third day—though in a few cases even earlier—that this primary dominant factor in plague shows itself. Instead of the infection remaining strictly localized within the lymphatic system, it becomes generalized through infection of the blood stream, owing to numerous direct communications that naturally exist between the lymph channels, on the one hand, and arteries and veins on the other, in the axilla, the side of the thorax, in the groin and other situations where buboes mostly predominate. In the case of deep abdominal buboes the veins become adherent to them, and thus direct infection of the blood is brought about. Once Bacillus pestis gains entrance into the circulation, it multiplies enormously, and rapidly becomes distributed throughout the internal organs, notably in the spleen and the liver. Masses of bacilli cause embolic infarcts in the organs, besides inducing terminal pneumonia. And as disintegration goes on simultaneously with multiplication, the liberated endotoxin simply floods the tissues, produces necrotic degeneration of the organs, and sets up hemorrhages from almost all hollow and solid viscera; profound changes in the finer elements of the nervous system occur from the toxin combining with the tissue cells, disorganizing their functions and laying in train the seeds of future mischief, the effects of which time and patience alone can eradicate.

The septicemia is generally of a progressive type, being most intense just prior to death; the number of organisms present in the blood may vary from 10 to 1,000,000 per cubic centimeter, and the growth of colonies on sloped agar from 0.1 c.c. of the blood may be few, fairly numerous, numerous, or very numerous, as classified by the Plague Research Commission.[8]

The development of septicemia can only be positively confirmed by bacteriological examination of the blood by culture, as the microscope fails to give any positive indication except in about 17 per cent. of such cases. The clinical signs, however, in about 72 per cent. of these cases raise a strong presumption of its presence; these consist in a quick, thready, compressible or almost imperceptible pulse, accompanied by intense nervous prostration, jaundice, and rapid wasting of the muscular and adipose tissues of the face, the features becoming pinched and hollowed out, even in the course of a single night, together with hemorrhages from the stomach, kidneys, or intestines. *Per contra,* the condition of the patient in about 28 per cent. of such cases, even in spite of a profound septicemia, is apparently so favourable that the physician is often deceived; the prognosis suddenly and, indeed, without any warning becomes falsified within a few hours, as death takes place by rapid cardiac failure. About 85.5 per cent. of all deaths among septicemic cases occur within six to seven days of illness, and 14.5 per cent. thereafter. The average recovery rate among them varies from 3 to 4 per cent. only, as compared with 55 per cent. among the non-septicemic.

If the ultimate fate of the patient is to be decided by the first factor—cardiac failure through toxemia—his general condition becomes gradually worse after the evening of the third day, the temperature oscillates until death between 102° to 104°, the delirium becomes fierce or maniacal, requiring physical restraint; he refuses medicines and nourishment, and each act of struggle or restlessness adds to the efforts of the greatly embarrassed heart, until it eventually ceases to beat, the patient sometimes expiring in the course of or immediately after a violent attempt at exertion, engendered presumably through deficient oxygenation or air-hunger. On the other hand, if a septicemia is to be the determining factor, the struggle between its steady, onward progress and the defensive processes of the system is no less arduous or prolonged. The clinical features above described supervene, the temperature, however, affording no clue; terminal pneumonia, internal and external hemorrhages, a semicomatose condition or actual coma, end the scene within the first week. Whenever a septicemia is limited in extent or is controlled by the action of the antipest serum, and the life of the patient thus prolonged, he drifts into marasmus, which I have described fully in a paper read at the Bombay Medical Congress of 1909.[9]

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[8] Journal of Hygiene, Extra Nos. 1 and 4, being Reports on Plague Investigations in India, September, 1906, and May 1908.

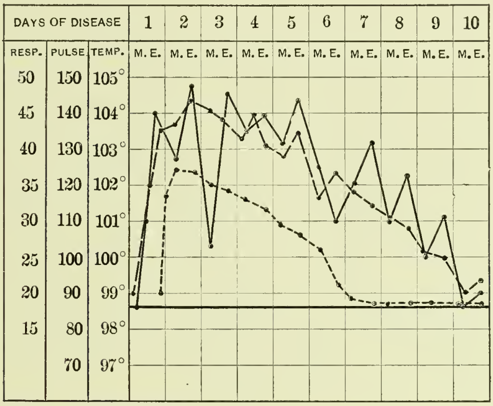

Fig. 1.—Chart of a normal case of plague of the bubonic type. (Solid line = temperature; dash line = pulse; dotted line = respiration. Same device in the other charts.)

If the patient is to recover, the further progress of the case is demonstrated by the accompanying chart (Fig. 1). After the lapse of forty-eight to sixty hours or longer since the evening of the third day, that is, by the sixth or seventh day, a gradual but perceptible change for the better becomes evident. The temperature slowly declines, there is amelioration in the general condition, the pulse improves in volume and tension, and the bubo or buboes become more circumscribed and prominent from commencing necrosis and suppuration. The pyrexia terminates by lysis, by short elevations and remissions, until it reaches normal on the morning of the ninth or tenth day, the tongue gradually clears, the appetite returns, the patient's appearance is brighter, and a very hopeful sign—he commences to grumble about something or other, or everything imaginable. Should the buboes suppurate, incision is required. The curve of temperature in a normal and uncomplicated case is thus limited to about ten days; occasionally it is shorter, but never less than eight days. It is usually divisible into three curves, the first terminating on the morning of the third day, the second on that of the sixth or seventh, and the third on or about the tenth day. This indicates that the disease is self-limited and bound to run a definite course, and that no abortive treatment can possibly deflect or modify its course except the early and liberal use of the antipest serum. Variations in the above curve are numerous: there may be but two only, or they may merge into each other; and, besides, complications, deep-seated buboes or their extension, or a succession of buboes in different positions, each ushered in by a well-marked elevation—all these render the curve unrecognizable except to an expert.

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[9] N. H. Choksy. On the Clinical Significance of Septicemia in Human Plague, Bombay Medical Congress, 1909.

II. The Cellulocutaneous Type. The development of the cellulocutaneous type is dependent upon the peculiar property of Bacillus pestis whereby its protoplasm or endotoxin is capable of setting up inflammatory and retrogressive changes of tissue elements, leading to progressive local necrosis. Klein[10] says, in reference to other organisms (but equally applicable to the bacillus plague), that the necrosis following typical symptoms of inflammation is the result of the local action of the bacilli, and so long as they are in sufficient numbers and of sufficient virulence, and so long as their multiplication proceeds, the necrosis of the tissues spreads into larger and larger areas. That is well exemplified in the case of the large necrosis often observed in plague.

Definite lesions at the point of infection exist in about 8 to 10 per cent. of cases, consisting in the development of phlyctenules, pustules, bullæ, and umbilicated bullæ. It is from the latter that this type originates. If the bulla is cut open or bursts of itself and the central core is removed, its point of attachment to the base appears as a small dark spot. It gradually increases in size until the whole of its base is encroached upon, and obliterated by a dark eschar. This continues to spread at the circumference from day to day until a period is reached when the medium suitable for the further multiplication of Bacillus pestis becoming exhausted, a line of demarcation appears. The eschar assumes a dark greenish hue, feels cold to the touch, is almost hard and leathery, and depressed in the centre, as if firmly bound down to the tissues underneath. Its spreading margin, somewhat higher, is conterminous with the surrounding skin, which becomes converted into a hard, angry, inflamed areola studded with minute vesicles; and often small, secondary necrosis is noticeable at some distance from the periphery through infection from the parent necrosis when it hapens to be extensive. Multiple umbilicated bullæ are also occasionally met with on different parts of the body surface, each giving rise to a small necrosis. If a little fluid be examined from the margin, it invariably shows a pure culture of Bacillus pestis. The destructive process, if limited, becomes a comparatively benign form of plague, to which I have applied the term "Cellulocutaneous Plague."[11] The buboes, if present—they are not invariably so—are secondary; and although, owing to the slowness of the process, the course of the disease is prolonged from two to three weeks instead of the normal period of eight to ten days, the recovery rate is higher. It is probable that recovery is determined, as Pescarolo and Quadrone[12] say in relation to Eberth's bacillus in typhoid fever, by the behavior of Bacillus pestis in the tissues in relation to the processes of infection and immunization, which differs, as we have already seen, from what it is when confined to the circulation; and in its conflict with the cellular elements of the tissues, immunizing bodies are produced which bring the infective process to a rapid termination. Should the necrosis become extensive, as in some cases it does, involving as much as sixty to ninety square inches of the body surface, the infection becomes generalized and the patient succumbs through septicemia.[13] Once the line of demarcation has formed, it is not difficult to remove the entire slough en masse, leaving behind a saucer-shaped depression in the subcutaneous tissue (often exposing the deep fascia and muscles) of gradually increasing depth from the periphery to the centre, filled with shreds of necrosed tissue, pus, and blood; it gradually assumes a healthy aspect under appropriate treatment. Such necroses have been observed on the scalp, neck, face, back, chest, arm and forearm, the abdominal wall, lumbar and gluteal regions, over the mammary gland, the vulva, and on the scrotum, the thigh, leg, and foot; in fact, wherever such umbilicated blisters might be situated The destruction of the soft tissues is often enormous, and large cavernous cavities exposing the bones of the face and head, involving exfoliation of the periosteum, and so also the cartilages of the ear, the eyelids, and the nasal bones. The upper and the lower jaws may be exposed when the process is confined to the head, neck, and face; the ribs may become exposed on the side of the thorax, and the testes if the scrotum is involved.

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[10] Brit. Med. Jour., August 4, 1900.

The clinical features are confined mainly to the local manifestation, its progress being marked by a slow and steady advance from day to day until the line of demarcation forms. The presence of buboes in direct lymphatic communication with the necrosis is dependent upon its extent. If the necrosis is small and less than a dollar in size, the buboes are more pronounced and the clinical phenomena almost identical with those observed in the bubonic type. Should it be larger—four to six inches in diameter—the buboes are of subordinate significance, inasmuch as the invasion being strictly localized, the general disturbance of the system is not so great and the result favorable. When the primary necrosis is at all extensive and oversteps the above limit, there are more chances of a septicemia developing, or, again, the patient may succumb through secondary infection or prostration, even after its excision.[14] The recovery rate is about 36 per cent., as compared with 25 per cent. in the bubonic type, and thus it constitutes the most benign type of plague.

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[11] Otherwise called carbuncles, and hitherto assumed to be a complication of plague; also known as pest necrosis.

[12] Zentralb. für inn. Med.; Brit. Med. Jour. (Epitome No. 292), November 14, 1908.

[13] It is also possible for septicemia to occur through the original bulla, before necrosis develops, as in Case No. 129, of 1908, at the Maratha Hospital.

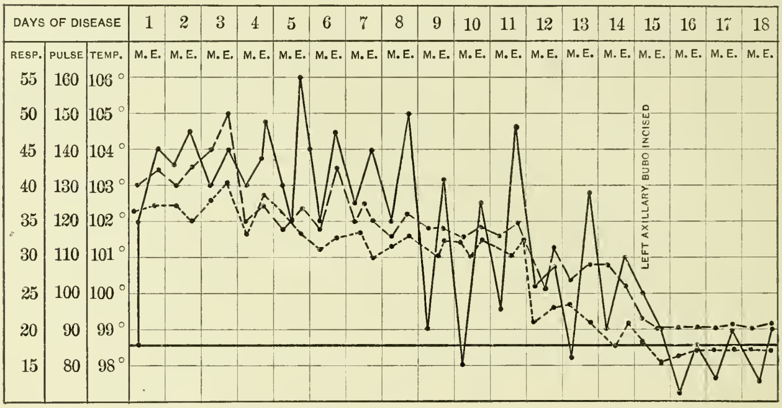

FIG. 2.—Chart of a normal case of plague of the cellulocutaneous type.

The accompanying chart (Fig. 2) illustrates the temperature curve of a case in which two necroses existed under the left costal margin, together with a bubo in the left axilla; the latter suppurated and was incised on the fifteenth day of illness. The course of the affection is seen to be prolonged to a fortnight, and the temperature curve is quite dissimilar to that in the bubonic type.

The accompanying photograghs (Figs. 3 to 8) demonstrate the varying extent of the necrosis in different cases.

III. THE SEPTICEMIC TYPE. The septicemic type owes its origin to primary infection of the blood, Bacillus pestis gaining direct entrance into the circulation.[15] The course of the affection is variable, extending from five to ten days. As in secondary septicemia in the bubonic type, a certain proportion of cases do not exhibit

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[14] N. H. Choksy. The Treatment of Plague with Prof. Lustig's Serum, Bombay, 1903.

[15] Malignant infection, with tiny deep-seated buboes and early septicemia, is liable to be mistaken for septicemic plague, the true nature of such cases being revealed only at the autopsy.

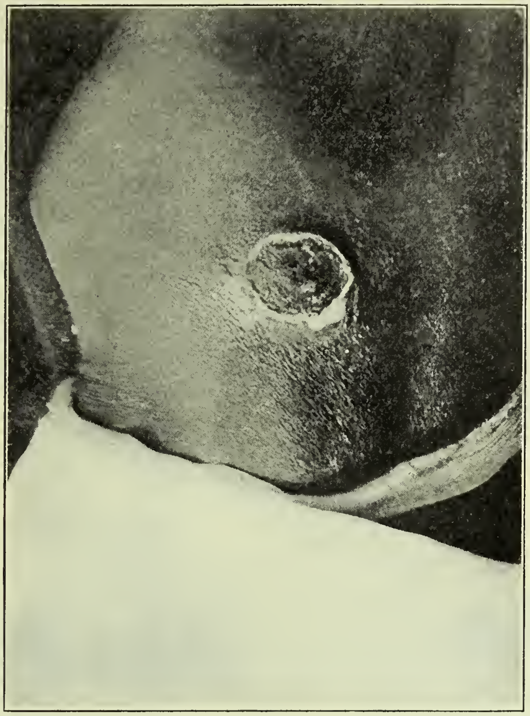

FIG. 3.—A small necrosis on the back in the lumbar region with secondary buboes in Scarpa's triangle; recovery.

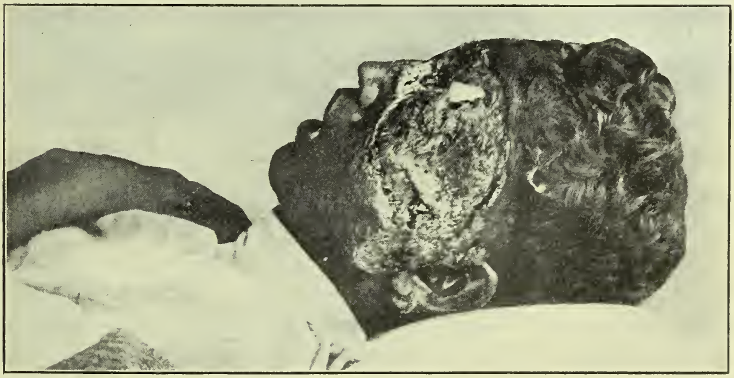

FIG. 4.—A large necrosis involving the forehead and side of the face over the temporal, zygomatic, malar, and nasal regions, with destruction of the upper and lower eyelids; recovery.

any clinical signs of grave systemic infection; so also there exist similar cases in the primary infection, in which, beyond a persistent high temperature with short morning remissions and evening exacerbations and a weak and frequent pulse, there is total absence of all grave symptoms: no jaundice, no wasting, no prostration, no delirium the mental faculties perfectly clear, and to all intents and purposes nothing apparently serious to bespeak a fatal termination within three to six days. And yet, such is the way in which they invariably terminate. The only possible means of diagnosis is by culture of the blood, which is not often undertaken until too late, and by the time it becomes confirmed the patient has succumbed through cardiac failure.

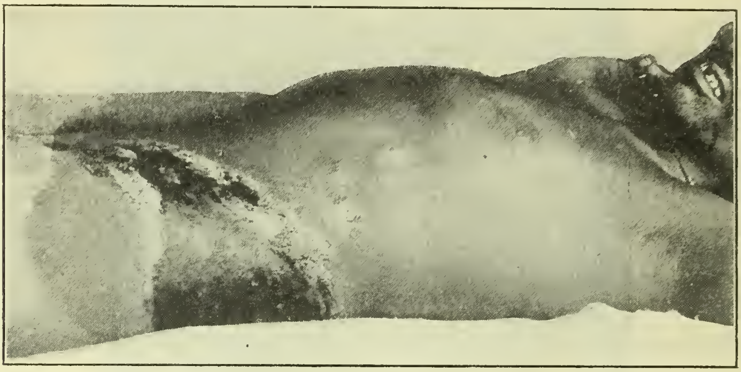

Fig. 5

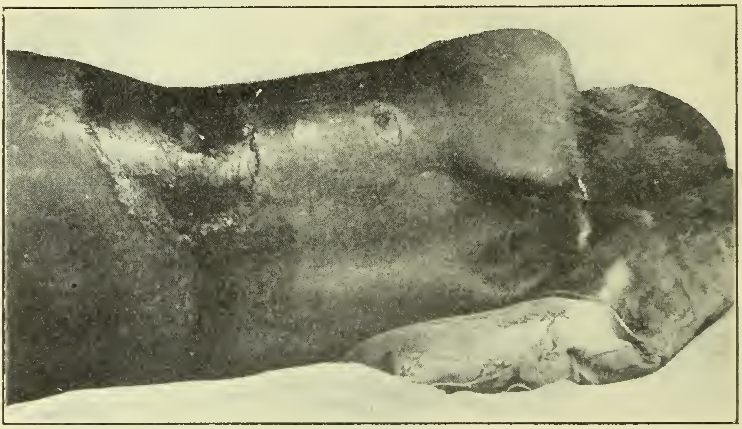

Fig. 6

Figs. 5 and 6.—Front and back views of an extensive necrosis, extending from the fold of the groin to the iliac crest, over the hip, and to the lumbar region, with small secondary necroses; fatal.

The accompanying chart (Fig. 9) illustrates the course of such a case with all the above characteristics.

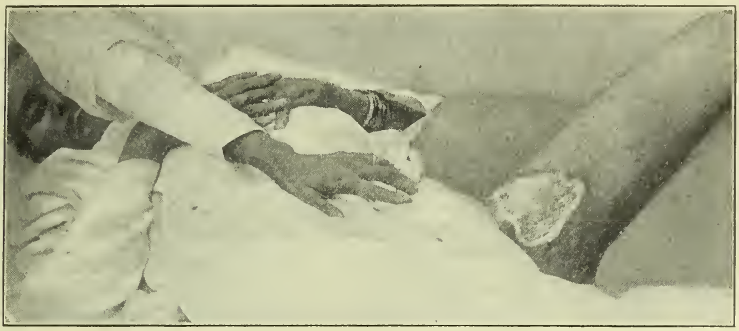

FIG. 7.—Secondary necrosis from the bubo infecting the subcutaneous cellular tissue in Scarpa's triangle; recovery.[16]

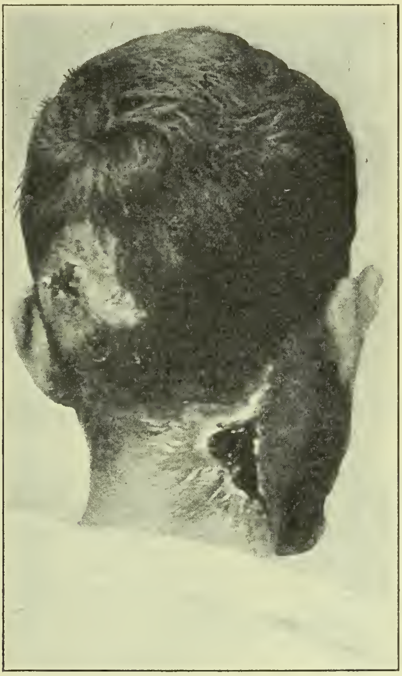

FIG. 8.—Wounds from two necroses, one on the scalp and the other on the side of the neck, in the process of cicatrization.

[16] Secondary necrosis from infection of the skin and subcutaneous cellular tissue by the bubo is occasionally met with, when the latter rapidly enlarges, comes up to the surface, and forms adhesions. It spreads similarly as the primary, and when the eschar is removed, the bubo is found to be firmly attached to its under surface.

By far the more common, however, is the type in which the symptoms are well pronounced at the very outset, the temperature usually following until the fourth day the ordinary course, as in the bubonic type, but variable thereafter. An extremely weak and thready pulse, intense and grave jaundice, profound nervous prostration, the limbs heavy and almost leaden, stupor or coma, the tongue brown, hemorrhages from the stomach, kidneys, or intestines, or subconjunctival, coldness of the extremities, and a few hours before death the appearance of one or more buboes in different parts of the body—such is the clinical picture exhibited. The only affection for which such cases are likely to be mistaken is grave spirillar infection in relapsing fever, but the absence of spirilla in the blood and the culture test confirmed the diagnosis. The following charts illustrate the course of such cases: Case No. 1721, of 1905 (Fig. 10), indicates the presence of severe melena causing collapse with subsequent reaction, and the development of femoral, inguinal, and iliac buboes on the morning of the day the patient succumbed. The other two cases, No. 838, of 1905 (Fig. 11), and No. 65, of 1904 (Fig. 12), show a somewhat more prolonged course, extending between nine to ten days, with the development of buboes on the seventh and ninth and tenth days respectively. In a few septicemia cases, however, the buboes appear on the third day of illness, the affection becomes partially localized within the lymphatic system, and recovery is just possible. But, on the whole, the fatality of these cases is so great that not more than 2 per cent. recover.

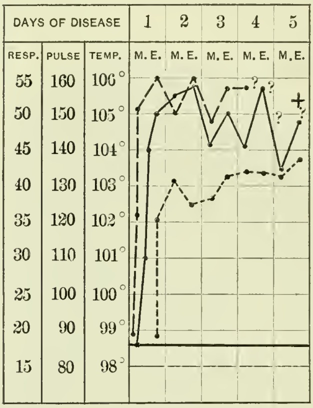

Fig. 9.—Chart of the septicemic type of plague.

IV. The Pneumonic Type. The most insidious and virulent and at the same time highly infective is the pneumonic type. The infection is usually contracted by inhalation of the fine spray of the infective sputum teeming with the bacilli. It is just possible that

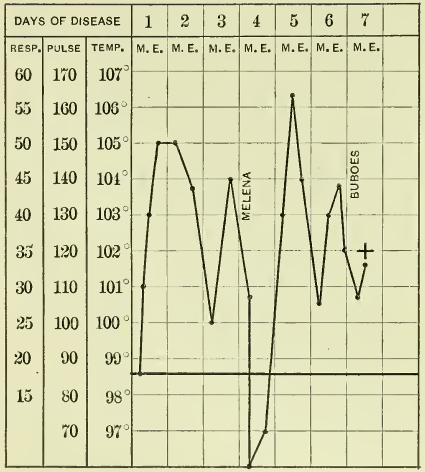

Fig. 10

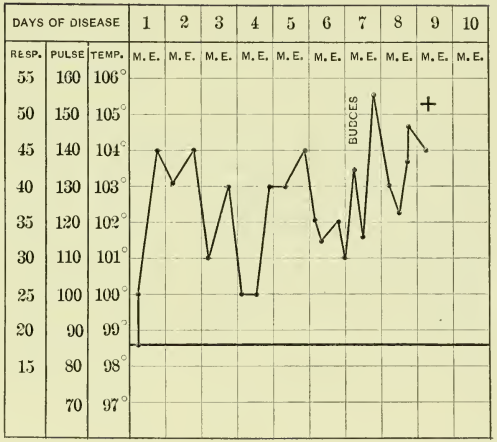

Fig. 11

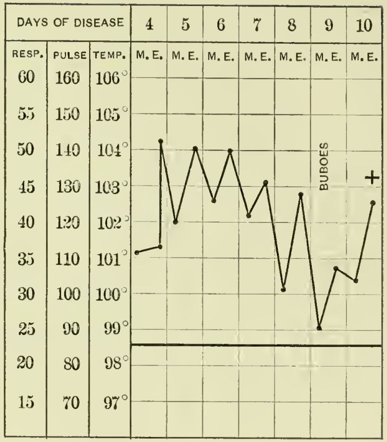

Fig. 12

Figs. 10, 11, and 12 —Charts of the septicemic type of plague to illustrate the presence of internal hemorrhage and the late development of buboes just before death it may be conveyed by the infected finger to the pharynx or tonsils, where a focus is formed, whence the lungs become infected. Or, again, the apparent primary pneumonia may be not really so, but a secondary development of malignant infection with deep-seated buboes, not felt during life-time, and early septicemia. The clinical picture of the type is masked in the early stages, and does not exhibit its full development until late. The course varies from three to five days, the termination being invariably fatal (Fig. 13).

Moderate fever, neither the pulse nor the respiratory ratio correspondingly higher; no physical signs, and yet marked prostration and aspect of grave illness; then, within a few hours, some scanty pellets of hemorrhagic sputum, followed by death within twenty-four hours, characterize the disease. The apparent initial mildness rapidly assuming gravity even without the appearance of the characteristic sputum is a pecular feature of the type. The sputum may be thick, viscid, almost or even purely hemorrhagic or thin and mucoid, tinged bright red; it may be profuse or extremely scanty, and brought up at long intervals. Simple microscopic examination of the sputum is extremely deceptive for purposes of diagnosis, as other organisms simulating the morphological characters of Bacillus pestis are not of infrequent occurrence. Many cases so diagnosticated have eventually proved not to be pneumonic plague. It is, therefore, absolutely necessary to make a culture and inoculate animals with it or with the sputum. If the animal responds to the usual tests, and plague bacilli are recovered from it, then only can the diagnosis be positive.

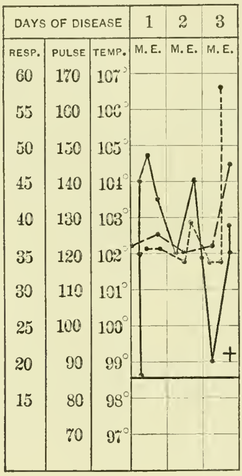

FIG. 13.—Chart of the pneumonic type of plague.

The rarity of this type and its great infectivity claim special notice. One single case is often the focus of a whole series of cases. The case of the late Major Manser, I.M.S., and his attending nurses; that of one of the former house surgeons of the Maratha Hospital, with its series of sixteen cases; that of one of the nurses at the Bai Motlabai Hospital, and of the student, both attending upon a case of the pneumonic type, who had miscarried, one and all terminating fatally, are sufficiently appalling. So far as regards Bombay. On the other side of India, Major Green and Dr. Justice[17] have recorded the history of the Baker-gunge epidemic of pneumonic plague, in which one case originating at Calcutta, in the house of Kaviraj Dwarkanath, led to a series of nineteen other cases, all of which proved fatal. Lieut.-Col. Crawford[18] has recorded another similar outbreak, involving twenty persons at Hughli, in January, 1905. In all the above instances the infective agent was the sputum of the patient, which induced a similar affection among others. Under other circumstances, however, especially if it happens to fall upon an exposed and inflamed mucous surface like the conjunctiva, it gives rise to bubonic plague. The saddest case of the kind that has come under my observation was that of one of the English nurses, at the Arthur Road Hospital. She had a severe catarrh with injected conjunctiva at the time. While bending over a patient to feed him, he happened to cough, and a drop of the infected sputum fell into the eye; three days later she developed plague with preauricular, parotid, and cervical buboes, with infiltration on the side of the infected eye, and eventally succumbed from œdema of the glottis.

No recovery from pneumonic plague in which the diagnosis has been confirmed as above has been hitherto recorded in Bombay. I have seen none in the course of twelve epidemics. I am, however, able to report one instance in which there was double infection of the lungs by Bacillus pestis and Bacillus pyocyaneus. The patient was admitted on the third day of illness—July 1, 1907—with moderate fever, 101.8°; pulse, 101, of fair volume; and respirations, 30; no physical signs and no sputum to indicate the nature of the case, except marked prostration. On the night of the sixth day, however, the temperature rose to 104.4°, the pulse to 130 and respirations to 35, and he developed symptoms of pain, tightness and constriction in the chest, dyspnœa, and cough, with scanty sputum, the naked eye appearance of which was characteristic neither of pneumonic plague nor of croupous pneumonia. It appeared to be somewhat dark and rusty, with a layer of greenish mucus, almost purulent. Physical examination revealed isolated patches of dulness in the middle region on both sides. A culture of the sputum was then made and sent to Dr. Ghadially, the Municipal Analyst, who reported three days later the presence of Bacillus pestis and Bacillus pyocyaneus in the culture, a little scraping from which was inoculated subcutaneously into a white mouse, and it succumbed within forty-eight hours and plague bacilli were recovered from it. There was thus no room for doubt as to the nature of the case. The patient remained in a rather precarious condition for three days, but improved thereafter, the temperature, pulse, and respirations gradually became lower, and when the sputum, which had in the meantime altered its character, was reëxamined on the eleventh idem, the thirteenth day of illness, there were no plague bacilli, but Staphylococcus aureus only; some of the culture from the sputum inoculated into a mouse did not kill it. In the meanwhile infection from the bronchial glands had spread to the deep abdominal and mesenteric glands, and pain, fixation of the abdominal wall, and tympanites developed, the course being subacute, without much rise of temperature after the seventeenth day of illness. Recovery, however, was gradual. In another instance there was double infection from Bacillus pestis and the pneumococcus, and it ended in recovery. Recovery is thus possible in cases of very moderate mixed infection.

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[17] Report of the Indian Plague Commission, 1902, p. 91, par. 203.

[18] Indian Med. Gaz., October, 1905.

V. THE AMBULATORY TYPE. The mild type of plague recognized as *Pestis ambulans* is characterized by moderate fever lasting for a few hours to a day or two, one or more small and tender glands, and hardly any constitutional disturbance. The patient may or may not rest; he usually works; and if the buboes get gradually absorbed, there is no other trouble. Occasionally suppuration takes place, whereupon he resorts to the hospital for relief.

Such, in brief, are the various types of plague and their principle clinical features as observed at Bombay. Whether the affection presents essential differences in its types and symptoms in different parts of the world owing to climatic, racial, or other causes, I must leave to others better qualified than myself to say. In so far as Bombay or Western India is concerned, those types prevail, but with a distinct racial incidence and fatality, depending to a great extent upon social conditions and environments. The greatest sufferers with the heaviest mortality rate (76.57 per cent.) are the Hindoos; the Mahomedans come next (68.52 per cent.), closely followed by the native Christians (65.80 per cent.); and lastly the Parsees (50 per cent.)[19] Europeans and Eurasians suffer so little in comparison that their statistics are scarcely worth comparing. The racial incidence of attacks also presents corresponding differences.

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[19] These figures relate to the actual case mortality rate recorded among 136,000 patients treated at the Arthur Road and Maratha Plague Hospitals during the twelve epidemics.

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IS SEVEN DAY FEVER OF INDIAN PORTS ONLY SPORADIC DENGUE?*

By Leonard Rogers, M. D., F. R. C. P., I. M. S.,
Calcutta, India,
Professor of Pathology, Calcutta Medical School.

The commonest fever of short duration in Calcutta among Europeans was only clearly differentiated from the nearly equally frequent malaria by me in 1905, and described (1) under the provisional title of A Peculiar Influenzalike Fever Prevailing in Calcutta. In that paper I discussed its differentiation from dengue, pointing out its resemblance to that disease in some respects, but concluded that it was more nearly akin to influenza. Early in the following year, in a paper (2) on Malarial Fevers in Calcutta and Their Differentiation from the Seven Day Influenzalike Fever I showed that the seasonal incidence of the seven day type of fever was the end of the hot weather and the rains, in which respect it differed totally from influenza (3), but agreed more nearly with that of dengue, and concluded "I am more than ever inclined to look upon seven day fever as distinct from any known disease."

A study of the literature of previous epidemics of dengue in India, especially those of 1824 and 1872, showed them to have been so closely in accordance with the textbook descriptions of the disease, and so widely divergent from the present distribution of seven day fever, that I could not see how they could

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*Read by title at the sixth annual meeting of the American Society of Tropical Medicine, Washington, April 10, 1909.

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be one and the same disease. Late in 1906 my friend, Captain J. W. D. Megaw, I. M. S., published (4) his personal experience of two attacks of the disease, and maintained that it was only a sporadic form of dengue, although no suspicion of this disease being so extremely common in Calcutta appears to have occurred to the succession of medical men who had served there, for I find by an examination of the clinical records back as far as seventeen years ago, that seven day fever was as common then as at the present day. A discussion on this point took place at the Medical Section of the Asiatic Society of Bengal, but the opinions of the numerous speakers were almost unanimous against Captain Megaw's suggestion. As I had never had an opportunity of seeing undoubted dengue, in order to get the opinions of some who were familiar with that disease, in 1907 (5) I brought up the subject before the London Royal Medical Chirurgical Society (now the Royal Society of Medicine) when Sir Patrick Manson said there could be no doubt seven day fever was quite distinct from dengue. I, therefore, described the disease as a definite disease in my work on *Fevers in the Tropics.*

Very recently Captain Megaw (6) has published a further lengthy communication in support of his view that the two fevers are identical, so it occurred to me that it would be of great interest and importance to obtain the opinions of the American Society of Tropical Medicine on this difficult point, for many of the members must be quite familiar with true West Indian dengue. I may mention that Lieutenant Colonel Pilghim, I. M. S., after experience of dengue in the West Indies, and some twenty years' knowledge of seven day fever in Calcutta, has informed me that he thinks they are clinically quite distinct. As I have fully described the Calcutta fever in the publications already referred to, it will suffice to submit some further recent temperature charts, and briefly discuss the main points in which the disease differs from the classical descriptions of dengue.

Epidemiology.—Good descriptions are on record of epidemic dengue in India (7), especially in the years 1824, 1872, and in Burma and Madras only in 1902. They all agree with the classical descriptions of the disease attacking almost the entire population of large towns within a few weeks or months, and causing great dislocation of business. Moreover, relapses were frequent during the same season, thus showing little tendency to produce immunity. These outbreaks also spread for one thousand miles or more inland in epidemic form. The Brisbane epidemic of 1905 (8) showed similar characters, and it was noted that an attack in the previous outbreak of 1897-8 had no or very little protective influence. Second attacks, at intervals up to three months, were often more severe than the primary ones. On the other hand, seven day fever of Indian ports is a sporadic disease of yearly occurrence every hot weather and rainy season as far back as hospital records can be obtained. It attacks a large proportion of newly arrived Europeans within the first two years of their residence, a second milder attack being occasionally seen one or two years after the first, but not, in my experience, in the same season, after which immunity appears to be largely developed. Apart altogether from the numerous differences in temperature curve, symptoms, and after effects, it is very difficult to see how true epidemic dengue can be converted into such a very differently distributed disease as that which I have described as seven day fever. When did the disease become sporadic? Was it after the 1824 or the 1872 epidemic, and if the former, how did the 1872 one affect nearly the whole population when all but the newcomers should have been immune after almost fifty years of "sporadic dengue"? If dengue does not protect against a second attack in the same season, or during the few years between the two recent Brisbane epidemics, how are persons attacked by seven day fever commonly immune after even a single attack? Again, true epidemic dengue in India spread widely inland over the country with great rapidity, yet seven day fever has only occasionally been met with beyond the great ports. So marked is this that an examination of three years' records of the large Lahore Medical College Hospital in the Punjab, and of the military hospital of a big station in the United Provinces, failed to reveal a single case. Once more, dengue equally affects Europeans and natives of India, while seven day fever is rare in the latter, although very occasionally seen in those who have come to Calcutta from distant places. A few cases of seven day fever occurring in the Punjab have been recently recorded as dengue, but I have frequently known persons attacked a few days after their return from Calcutta to inland towns, without the disease spreading there as elsewhere, as true dengue commonly does. The epidemiology of the two fevers is, then, widely different in every way, and from this point of view alone it is extremely difficult to see how one can be but a sporadic form of the other.

Pyrexia and Symptoms.—Only a few points can be dealt with under this heading within reasonable limits of space. Dengue has been described as a "three day fever" by Lichtenstein, although sometimes followed by a terminal rise of temperature about the sixth day of very brief duration and slight degree. Such was the type in Calcutta in 1872, when any return of the fever after the second or third day was exceptional in the recorded charts. Further, I can find in epidemic dengue records no description of the high continued temperature of seven days' duration, with the general appearance of typhoid patients, such as I have frequently met with, and have published charts of, in seven day fever. If this had occurred in 1824 it could not have been overlooked by such a careful writer on fevers of Bengal as Twining, who has left a masterly description of this dengue epidemic. If, then, seven day fever is but sporadic dengue, the disease must both have changed its type to an extent unknown in any other specific disease, but must also in passing

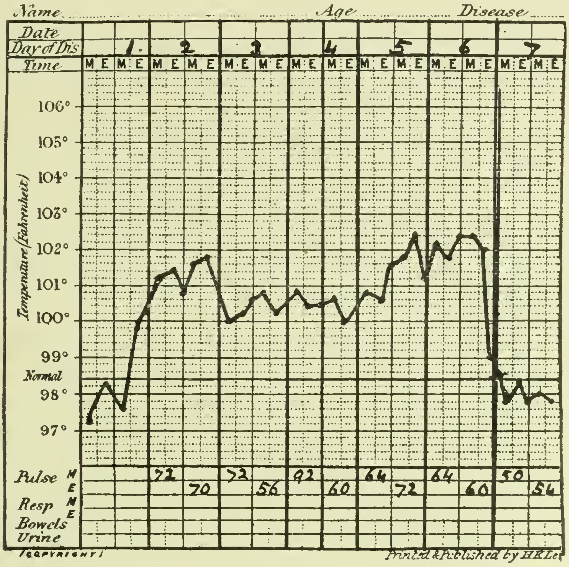

Chart 1.

from an occasional severe epidemic form to ever present sporadic one, have greatly increased the duration and height of the temperature curve, instead of becoming much milder as in other known instances, such as the decimating epidemics of measles in Polynesia and its comparatively mild sporadic form in European countries. This is contrary to all known laws of such diseases, and appears to me to be fatal to such a contention. It is true that Captain Megaw holds that both the three day fever of Chitral, described by McCarrison (9), and seven day fever of Indian ports, are both dengue, but he does not attempt to explain why the disease nearly invariably runs a short course in one place and a long one in another. Such a view would make dengue yet more protean and variable in character, which to my mind is much less likely than that these Indian types are distinct fevers, which have been sometimes confounded with dengue when unusually prevalent.

After Effects.—One of the most characteristic features of classical dengue is the excruciating character of the pains during the disease, requiring morphine frequently for their relief, and their persistence for weeks or months after the fever has left. This feature was well marked in the Indian epidemics, for Twining records that in 1824 protracted debility, long continued pains in the ankles, and dull, aching pains in the joints of the fingers and toes, were almost invariably complained of for many weeks after the cessation of the fever, and E. Charles wrote to the same effect of the 1872 outbreak. I accidentally met with a European lady recently who suffered in that epidemic, and without any prompting on my part she began to dilate on her terrible sufferings over thirty years before. This noteworthy symptom is conspicuous by its absence in seven day fever, in which the pains are little more than in influenza, and do not persist after the fever has subsided, and even not recur with the prolonged terminal rise of temperature.

The outbreak recently described as dengue by Ashburn and Craig (10) in the Philippine Islands is certainly much more like Calcutta seven day fever than classical dengue, but is it not possible that it is the same fever as that so commonly met with in Indian ports, and not true dengue? This view is supported by the recent work of R. Doerr (11) on a three day fever in Southeastern Europe, for in both instances an invisible virus, which passes through a

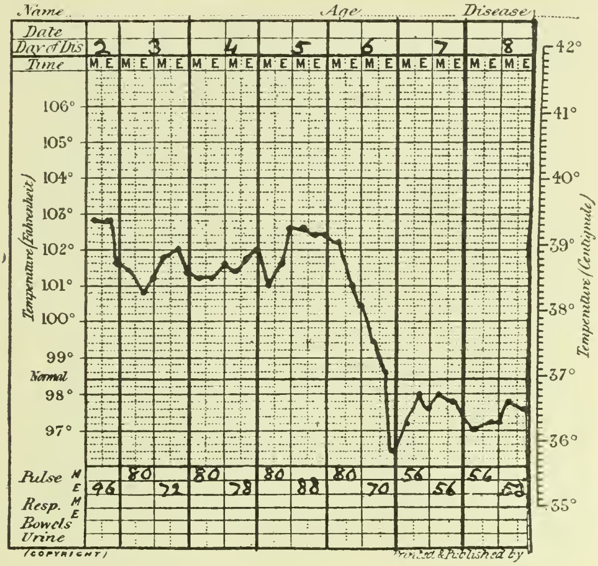

Chart 2.

very fine porcelain filter, has been proved to be present in the blood, yet the European three day fever does not appear to have resembled dengue, or raised only suspicion of the occurrence of that disease.

In the absence of any accurate knowledge of the causative organisms of these various fevers, the questions here discussed are not likely to be easily settled, but I shall await with much interest the opinions of the society concerning them.

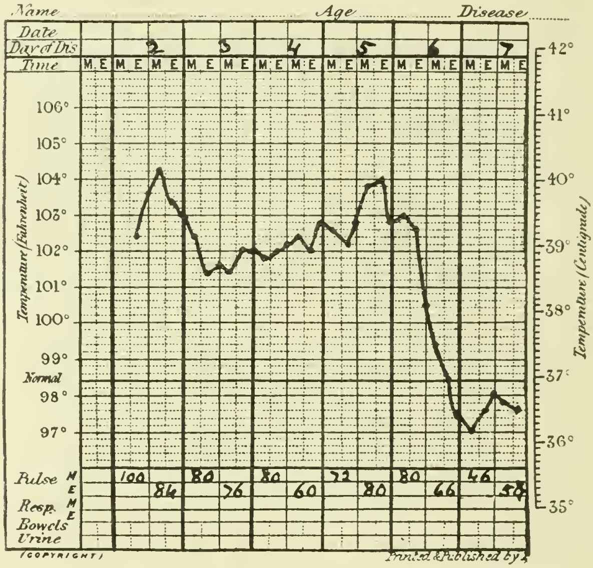

Chart 3.

Temperature Charts.—The accompanying charts illustrate the type of the fever in its different degrees. Chart I is that of a European attacked while in a hospital, so that it shows the whole course of the disease, and demonstrates that it is essentially a short continued type, with exacerbations at the beginning and the end. The slow pulse is also a most noteworthy feature, having been only 60 with a temperature of over 102° F. at the end. The rise is rapid and the fall equally so.

Chart 2 is that of a European male admitted on the second day of the fever, which ran a high continued type with but a very slight rise at the end. The pulse is again slow, and such patients frequently have the flushed appearance of early typhoid and occasionally also show slight abdominal distention, the rapid fall on the sixth or seventh day only removing the strong suspicion of that disease. I have not met with any descriptions of this typhoidlike

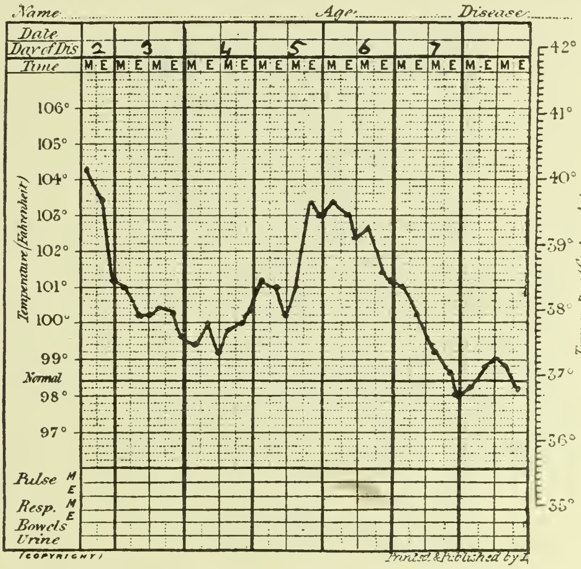

Chart 4.

type in accounts of epidemic dengue, although it is quite common in Calcutta seven day fever, and appears to me to be a very important point in the differentiation of the two diseases.

Chart 3 shows a very similar, but yet higher, continued type with distinct preliminary and terminal rises producing a slight saddle back remission between them, and a slow pulse, except immediately after admission.

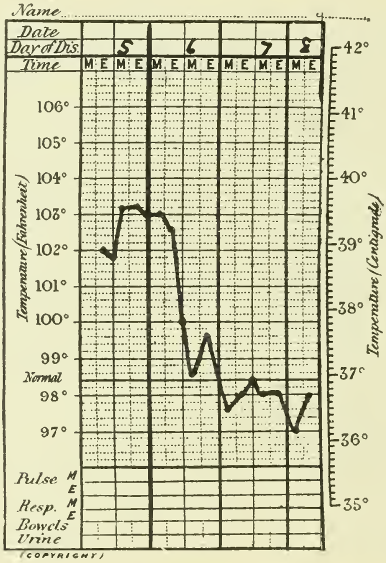

Chart 5.

Chart 4 shows a much more marked saddle back remission to only a little over 99° F., and all intermediate curves between this and Chart 3 occur, and constitute the most striking feature of the general run of cases. It is rare, however, for the temperature to fall actually to or below normal. The terminal rise is a prolonged and high one, much more so than in classical dengue.

Chart 5 is that of a man admitted on the fifth day during the terminal rise. These cases constitute a large proportion of the admissions for seven day fever, and unless the history is carefully ascertained, may easily be mistaken for a short two or three day fever. These cases were commonly mistaken for malaria in Calcutta before I described this fever, but may almost invariably be at once distinguished from it by the characteristically slow pulse during the terminal rise of seven day fever. The fact that about half the admissions in the European hospital, even among sailors, are first seen at this late stage of the disease, is a striking fact, again differing widely from dengue, in which the onset is usually so very severe as at once to bring the sufferers under medical treatment. I have myself worked through a fairly mild attack of seven day fever with only a feeling of general slackness and some headache, although as a rule frontal headache and pains in the loins and limbs are well marked features of the infection, much as in influenza. These charts will serve to convey a general idea of the disease, and enable it to be compared with undoubted West Indian dengue.

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Extracted from the American Journal of the Medical Sciences, September, 1909

LEPROSY IN THE PHILIPPINE ISLANDS AND ITS TREATMENT.[1]

By Victor G. Heiser, M.D.,

PASSED ASSISTANT SURGEON, U. S. PUBLIC HEALTH AND MARINE HOSPITAL SERVICE; DIRECTOR OF HEALTH AND CHIEF QUARANTINE OFFICER FOR THE PHILIPPINE ISLANDS, MANILA.

Notwithstanding the comprehensive title of this paper, it is not my intention to discuss the history of leprosy in the Philippine Islands any farther back than the beginning of American occupation, because that is not essential to the practical questions under consideration, and it has already been done in one of my previous papers.[2]

At the beginning of the period with which this paper deals there were in the Philippines, according to the best record obtainable, between 3500 and 4000 lepers. While it is true that many of the reported cases were, on the application of more accurate diagnostic methods than had at first been employed, found not to be cases of leprosy, there were enough obscure cases overlooked to contraindicate any revision of the figures. There were never any grounds for the estimates ranging from 10,000 to 30,000, which were given circulation in the earlier days of the new regime.

The attempt at partial segregation of the worst cases, which in Spanish times had been begun and carried on by the church authorities as a matter of charity rather than legal proscription, was continued by the Americans, both before and after the establishment of civil government; but a systematic plan which had for its object the reduction of the number of new infections and the ultimate eradication of the disease from the Islands was not begun until 1905, although the island of Culion was selected for this purpose as early as 1901.

This island is well isolated, is roughly 20 by 40 miles in size, and is located about 240 miles from Manila in a southwesterly direction. The lepers are permitted to establish themselves at any place on the island, and if they desire to follow agricultural pursuits, the necessary animals and implements are provided at Government expense. In actual practice, however, it is found that they practically all live in the town of Culion, where everything is furnished for them by the Government. A large modern hospital has been established for those who are bedfast or those who desire to undergo special treatment. The town is located on an elevated site, has a modern water and sewage system, and is practically controlled by regulations and ordinances which the lepers themselves make. If the work of collecting lepers could have been rushed through with military rigidity, the problem would have been very much simplified, but it was deemed advisable to precede the collection of the lepers by a campaign of education and thereby secure the coöperation of the public rather than its opposition.

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[1] Read by title at the sixth annual meeting of the American Society of Tropical Medicine, Washington, D. C., April 10, 1909.

[2] Leprosy in the Philippine Islands and the Present Methods of Combating the Disease, Medical Record, June 8, 1907.

After this preliminary work, the plan adopted and still followed, which the geography of the country so eminently favored, consisted in removing all leprous patients from the well-isolated islands which contained only a few victims, and subsequently recanvassing the territory two or more times for cases which might have escaped, been overlooked, or which subsequently developed. By the method pursued the greatest amount of territory was freed in the shortest possible time. In military phraseology, the outposts were captured first and the lines gradually moved forward to the strongholds.

Experience has shown that when all of the native lepers have been removed from an island, the people of that island may be safely trusted with the duty of keeping foreign lepers from taking refuge there. The better points of human nature are being utilized in the campaign and often times prove valuable weapons.

Commitment to the Colony does not mean permanent separation from friends and relatives, since provision has been made for restricted visiting under proper safeguards from a neighboring island, on which the non-infected are permitted to camp or to live permanently if they desire, in order that they may be permitted to visit their friends and relatives. The law under which the policy of segregation is carried out probably vests more absolute power in the director of health than the laws of other states or countries. Briefly, he has authority to cause to be apprehended every person who is believed to be a leper, and to detain them if the bacillus of the disease can be demonstrated. Furthermore, it is the duty of all officials and others to report to the director of health any case of leprosy that comes to their knowledge. Failure to do so is punishable by fine.

The results of the segregation policy so far have been very encouraging. On February 1, 1909, according to official figures, there were only 2291 lepers in the Philippine Islands, which fact demonstrated that since May, 1905, when effective segregation was begun, the number of deaths has exceeded the number of new cases by 1409. The falling off in the number of new cases is one of the most encouraging evidences of success. It is estimated from the data on hand that under the old system there were about seven hundred new infections annually. During the past year there have not been more than 300 new cases, a difference of about 57 per cent. If these results can be brought about by incomplete segregation, it can readily be seen that the prospect of ultimately reducing the number to insignificant proportions is very encouraging.

In an address before the Philippine Islands Medical Association, more than two years ago, I held that whatever may be the views of well-informed persons with regard to the communicability of leprosy, and however widely eminent medical men may differ upon this question, the incontrovertible fact remains that every leper who is capable of giving off lepra bacilli is at least one centre of infection, and that it is an utterly hopeless and useless undertaking to attempt to eradicate the disease without removing the source from which it is transmitted; and I asked that prophylactic medicine should not be turned aside by a few sentimentalists from its march to a goal which offered the magnificant hope of the complete eradication of this plague from the face of the earth and the saving of many innocent human beings who are now sacrificed annually to this most loathesome disease through sheer sentimentality. As more and more experience becomes available, these views are constantly strengthening, and it is believed that the cases which cannot be traced to another case are very few.

The most important factor now in connection with the work in the Philippines is early diagnosis. The earliest and most constant symptom observed is a nasal ulcer which is situated on the nasal septum at the junction of the cartilaginous and bony portion. Among 1200 cases taken in regular order at Culion, these ulcers were noted in 799. It is my opinion that if the remaining septums had been examined microscopically, scar tissue would have been found which would be strongly presumptive evidence that ulcers had existed previously. My experience in the examination of more than two thousand Philippine lepers and of those of Hawaii and of the Louisana colony near Bruns, confirms the importance and constancy of this sign, which may often be found long before there are any other objective or conscious subjective symptoms. Writers on leprosy give the incubation stage as from three weeks to twenty-seven years. No reliable data have become available here to prove or disprove this theory. Several Americans, whom it is fair to presume were not exposed to the disease in the United States, were found to have the disease within two years of their arrival in the Philippines.

Its extent and effect in different individuals or in the same patient at different times is very variable. I have seen a number of microscopically positive cases in which the only clinical symptom was a nasal ulcer, perhaps very obscure and innocent looking. Such cases usually come from houses in which advanced cases have existed. For this reason it is customary to have those who have been in contact with bad cases examined for this sign and scrapings submitted to a microscopic examination. The precautions enjoined at the leper institutions under the bureau of health is to protect the nasal mucous membrane as a first consideration, giving second place to, but not under-rating the old-time precautions. The membrane of the nose is easily protected by nasal plugs of sterilized absorbent cotton.

With regard to the types of the disease in the Philippine Islands, a fair estimate may be found from the fact that of 1200 cases studied in the order of admission, 374 were of the anesthetic type, 157 of the tubercular type, and 650 partaking of the character of both, or mixed cases. It was observed that in a majority of cases the integrity of the eyebrows was disturbed. Among the 1200, the eyebrows had been entirely destroyed in 264 cases, and in 599 cases they were half gone. In the remainder of the cases there was generally some impairment of the appendages sufficient to constitute some degree of expressional deformity.

TREATMENT. As health officers, we are naturally more interested in preventing the disease and in the protection of the public than in the care or relief of the individual, yet no remedy within the realm of reason, whether physiological or empirical, has been neglected. Potassium iodide, mercury, creosote, salicylic acid, chaulmoogra oil, gurgon oil, leprol, nastin "B," experimental sera, and the *x*-rays have all been tried without curative effect, except the *x*-rays, which have proved successful in a few cases, but from our present experience can by no means be regarded as being suitable as a routine treatment. The cases in which they are apparently of value is in the early stage of the tubercular type in young and otherwise healthy subjects. The breaking down by the *x*-rays of one large, leprous granuloma of an individual usually results in marked coincident improvement in the granulomas situated in parts of the body far removed, and to which the *x*-rays have not been applied. One of the cases successfully treated by this method was recently reported.[3]

San Lazaro Hospital at Manila was the first institution in the world to use the *x*-ray treatment for leprosy with any degree of success, but this was probably due to the fact that there were a larger number of cases to choose from and the particular type which yielded to this form of treatment came under observation early. Chaulmoogra oil so far has not proved of value, but owing to the excellent results obtained in Louisana by Dyer with the crude oil, another thorough test of this treatment is being made.

CONCLUSIONS. 1. The experience in the Philipinnes during the past three years demonstrates that segregation has decreased the incidence of leprosy by over 50 per cent.

2. Of all the treatments tried, the *x*-rays is the only one which produced a cure, but as yet it is suitable only for specially selected cases.

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[3] Preliminary Notes upon a Case of Leprosy apparently Cured with the *x*-Rays, Medical Record, October 31, 1908

Reprinted from the New York Medical Journal for July 10, 1909.

A NOTE ON THE IPECAC TREATMENT OF AMŒBIC DYSENTERY.*

By George Dock, M. D.,
New Orleans,
Professor of Theory and Practice of Medicine in the Tulane University of Louisiana.

(*Published under the Imprimatur of the American Society of Tropical Medicine.*)

The ætiology of the disease usually called amœbic dysentery is still unsettled, but as a practical matter we know that when amœbæ of certain kinds occur in the stools there is a peculiar form of ulcerative enteritis, affecting part or even all of the colon. We also know that the affected individual is likely to have a chronic, recurring diarrhœa or dysentery, with considerable risk of large abscess of the liver, or of other complications. Like many other diseases, it is relatively amenable to treatment in the beginning, and this fact, with its tendency to remissions, make it a favorable subject for therapeutic novelties, most of which fail in longer trials. Ipecac has been used from an early period, but although it is still recommended enthusiastically by many, it is either not tried, or used with poor, or indifferent results by many more. Even those who employ it with confidence differ as to the class of patients most benefitted, some stating that the remedy is only useful in acute cases, others chronic ones; some in the amœbic, others in the bacillary

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*Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the United States Naval Medical School, Washington, D. C., April 10, 1909.

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forms. Having used it with what seemed to me remarkably good results in chronic amœbic dysentery, and having learned some things about its employment and action that are not widely known, it may serve a purpose to call attention to it at this time.

I have no theory of the action of the drug. I have made some experiments with live amœbæ from stools, on the warm stage, which suggest a direct destructive action, and I hope to carry the observations farther. There is also, apparently, a cholagogue action, and sometimes a purgative action, but I am unable to ascribe what part, if any, these have in the general result.

Clinically, in cases treated with ipecac, we see within a few hours a cessation of the amœboid motion of the parasites. Soon after, they have the appearance, in fresh stools, of amœbæ that die under observation, and in from one to three days they disappear completely. In the same time, beginning within twelve hours from the administration of ipecac, the stools lose their dysenteric character. Mucus and blood, later pus, disappear, and the stools resemble those of mild, simple enteritis, or normal infants' stools, or even become formed. Sloughs and the gangrenous or cadaveric odor also disappear, except in the extensive and severe cases sometimes encountered, in which the disease is too advanced to permit time for improvement. Other protozoa in the fæces, such as trichomonata, vary much in their reaction to ipecac. Sometimes they disappear before the amœbæ; usually they are little or not at all affected. In one case the interne, Mr. Kory, showed me a lively strongyloides in a stool passed after all the amœbæ were killed. Griping and tenesmus sometimes continue a short time, but soon cease, and are rarely increased by the treatment, Most of my observations were made in cases in the wards of the Charity Hospital, New Orleans, within the current year, and as many of the patients left as soon as they got relief, the final outcome cannot be stated. In two cases the patients remained in the hospital for four and two months respectively after treatment, and control observations, after salts and with the use of the rectal tube, have been negative. Similar experiences have been met by several of my colleagues who have used the treatment.

The suggestion to try the method was given me by seeing, in the summer of 1908, a patient treated in my wards four and a half years before. He had had a severe dysentery for two years, acquired in the Philippines, but remained free from symptoms and amœbæ after ipecac treatment. The case will be reported by my former colleague, Dr. John G. Gage, of Ann Arbor.

In another case cure has continued for six months. A brief history will be instructive, and I have to thank my friend, Dr. H. A. Freund, of Detroit, Michigan, who carried out the final treatment, for notes of the latter and its results.

The patient was a white male, who at the aged of fifty-two acquired chronic dysentery in Honduras, in March, 1904. He treated himself by daily enemata of physiological salt solution, two quarts, followed by a quart of water containing five grains of quinine. Notwithstanding this treatment and a careful life in other respects, I found in December, 1904, a moderately severe dysentery, with mucus, blood, and pus, and large, active amœbæ with red blood cell inclusions. For the next three and a half years the patient carried out treatment with saline enemata, followed by 1 in 1,000 quinine solution. He became very expert in taking the injections, and by posture got them well up in the colon and retained the quinine for considerable periods. He also took, all this time, chaparro amargosa, and also sulphur, the latter in twenty grain doses, three times a day. He was satisfied with his condition, and though not well he was fairly comfortable until September, 1908, when, possibly as a result of a chilling, he had a pain in the left side, and frequent small stools. He then came to see me. Examination with the proctoscope showed general redness and swelling of the mucosa, with many small ulcers. Bits of rose colored mucus lay on the surface, and showed under the microscope large numbers of large and active amœbæ. Dr. Freund then began ipecac treatment, and owing to the abrupt exacerbation and the long duration it seemed advisable to make it thorough. After the first course of thirteen five grain pills of ipecac, salol covered, in as many hours, there was still considerable mucus in the stools but the amœbæ were all dead. Two more courses of ipecac were given, ice water and quinine enemata used, and the patient not allowed to go about for six weeks. The ulcers in the rectum were touched with silver nitrate

Certain details of the treatment should be considered. The patient should be kept in bed, not only on account of the depression sometimes but not always caused by the ipecac, but on general principles that apply to the treatment of all severe intestinal inflammations. With the idea of getting the remedy as closely as possible in contact with the parasites, there should be a preliminary purgative. Epsom or Glauber salts, with or without a preliminary dose of calomel, seem well adapted. Fasting beforehand is rarely necessary, but all food should be stopped while the ipecac is being taken, and only liquids, such as albumen water, gruel, whey, weak tea, and water, used after it.

The dose of ipecac may be varied to suit the severity of the case, from thirty to sixty grains being given at first, and then twenty to forty grains twice a day, for three days. At first I gave five or seven and a half grain doses every hour until from sixty to 105 grains were taken, but it seems equally efficient and less troublesome to give a larger dose once or twice a day. In some cases the condition of the stools and other symptoms warrant stopping treatment before the end of the third day. The ipecac is given in pills covered with salol or keratin. The latter I have never used, because the salol covered pills are easily made by any competent pharmacist, and are usually satisfactory. Dr. Freund has had some made with chocolate coating under the salol. The object of the cover is to prevent an emetic action, salol and keratin being undissolved in the stomach, and this makes unnecessary the use of opium preparations, formerly thought to be essential in the ipecac treatment. If there is much pain morphine may, of course, be used, but I cannot but think it a mistake to narcotize a patient with dysentery. Vomiting rarely occurs after taking ipecac as described. Usually there is no nausea or regurgitation at all, and several patients have assured me they had no unpleasant sensations of any kind. Rarely there is vomiting after the first dose. In one case a patient taking ten grains three times a day vomited if his mealtime came two hours after the medicine, but not when the hours were changed. Occasionally, more or less distinct salivation is noticed. As a precaution, I advise patients to lie down after taking the ipecac, on the right side, with an ice bag to apply to the epigastrium or throat in case nausea appears. The patient must always be warned not to chew the pills, but in children, and patients who do not understand well, this may occur, with the result of an emetic action. Griping after ipecac may be treated by a hypodermic injection of atropine. Diarrhœa persisting after the treatment, and after the amœbæ have disappeared, should be treated as under other conditions, but not with strong astringents or opiates. When in doubt in such a case; a saline purgative is the best thing to use. Hot normal saline flushes of the colon, or ice water, are valuable in the after treatment. Local treatment of ulcers of the rectum should not be neglected, if found, and they should always be looked for.

Perhaps it may be necessary to say that I claim no credit for originality in any of the details given, and wish only to stimulate others to actual trials, as well as to the study of the recent literature.

124 Baronne Street.

Reprinted from the New York Medical Journal for July 10, 1909.

Discussion.

Dr. STITT said that in the Philippines most excellent results were obtained by the use of ipecac, so that the surgeons on the ships began giving it as soon as the men showed symptoms of dysentery. When a man came to the hospital no motile amœbæ could ever be found. In order to discover these, the hospital physicians had to ask those outside not to give ipecac before the men entered the hospital. Dr. Stitt said that he had had an amœbic affection for two or three years, and that the only thing that would do him any good was ipecac. After using this for three or four days, however, it would cause him to lose his appetite, and he would then have to stop taking the drug.

Dr. ANDERS asked whether Dr. Dock had met with any patients who were cured. Some years ago he had come to regard ipecac as a specific, but more recently he had had under observation a patient in whom ipecac produced only an apparent cure. The patient returned a few months later, and this time the ipecac treatment failed. Irrigation with quinine seemed to do more good, but soon became ineffective. Finally he tried irrigation with quinine and copper sulphate alternately. That seemed to do the most good, though a few amœbæ remained. Enterostomy was then done, and the bowel irrigated from above. The patient, who was an intelligent man, regarded himself as perfectly well after this, though he still showed some *Amœbæ dysenteriæ* in his stools.

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Discussion.

Dr. Ashburn said that he had begun to use ipecac for dysentery in 1897, and had continued to use it ever since in acute cases. He had seen only two cases that did not promptly end in recovery under the ipecac treatment, if the patient retained the drug. If the patient could not retain it, the disease occasionally went into the chronic form. If he could not cure amœbic dysentery within a month, he felt doubtful of ever curing it. Although he had seen benefit from the use of ipecac in chronic cases, he thought that the benefit was usually temporary, but he believed this temporary benefit from ipecac to be more than he could obtain from other remedies.

Dr. Dock, said in answer to Dr. Anders's question, that a good many of his patients had left the hospital immediately, and he had been unable to follow them up. He considered ipecac more effective at once than any other drug, and he had had rather better results in cases of long standing than with any other drug. Two of his patients had been taking what was thought to be the most efficacious treatment except with ipecac, namely the quinine irrigations.

A BIOGRAPHICAL SKETCH OF AZEL AMES, M. D.*

By JOHN M. SWAN, M. D., Philadelphia
SECRETARY OF THE AMERICAN SOCIETY OF TROPICAL MEDICINE

AZEL AMES was born in Chelsea, Mass., August 16, 1845. After completing the course of study offered by the public schools of Chelsea, he entered Phillips Academy at Andover. His school and academy days were spent during one of the most serious political periods in the history of any nation. The arguments for and against slavery and concerning the right of secession made a very great impression on his mind, as they did upon the mind of every inhabitant of the United States. The outbreak of hostilities between the two sections of the country occurred when young Ames was in his seventeenth year. He wanted to join the Army; but his father was unwilling that he should enlist as a private soldier on account of his age. He had already expressed a desire to study medicine and was preparing to enter the Medical Department of Harvard University. His father was urgent that he persist in this already planned course. The combined spirit of the time and the enthusiasm of youth succeeded in overcoming the parental objection and he enlisted in the Hospital Corps of the Federal Army on September 2, 1862. In a little more than a month he was promoted to the Hospital Steward; his warrant bearing the date of October 15, 1862, one day less than two months after he had passed his seventeenth birthday.

His first duty was performed in the hospitals about Washington. Early in 1863 he was ordered to New Orleans as aid to Col. Peter Pineo, Medical Inspector of the Department of the Gulf. On August 18, 1863, he was discharged and was immediately commissioned first lieutenant of engineers, being mustered in thirteen days later, August 31.

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*Read at the Sixth Annual Meeting of the American Society of Tropical Medicine, held at the United States Naval Medical School, Washington, D. C., U. S. A., April 10, 1909.

During this tour of duty he had his first experience in tropical medicine. In the swamps of Louisiana, on the Mississippi River, and on the numerous bayous emptying into the river he made the intimate acquaintance of the anopheles mosquito, and was obliged to resign on account of his malarial infection in November 10, 1863.

Upon regaining his health he completed his studies preparatory to medicine and entered the Medical Department of Harvard University, from which he was graduated with the degree doctor of medicine in the class of 1871. After his graduation he started to practise medicine in Wakefield, Mass. He at once became more interested in sanitary science and engineering than in the work of a general family practitioner, and it was in the former branches that the greater part of his professional activity was centered. While practising in Wakefield, in 1872, he framed the Code of Health Regulations for the town. He was instrumental in creating the first independent Board of Health of Wakefield, of which he was the secretary and executive officer for a number of years. In 1873, he advocated the installation of a public water supply and was one of the original board of directors of the company, which was organized to supply Wakefield with water. During this period he was moderator of the town council on various occasions, and served on numerous special committees which were entrusted with the details of the business of the community in which he lived. Many of the reforms and improvements in the manner of conducting the public business in Wakefield originated in the Review Club, of which Dr. Ames was one of the organizers. This club apparently reviewed the needs of the town, the deeds of the prominent people of the town, and the activities of other communities. By means of the Review Club lectures and of the publicity accorded by the purchase of a newspaper, the Wakefield *Citizen and Banner,* of which Dr. Ames was editor for several years, public opinion was influenced in the direction of better town administration.

In 1878 he was elected a representative in the State Legislature of Massachusetts, and while attending to the duties of this office in Boston he was instrumental in defeating a bill which was intended to limit the facilities for the teaching of anatomy in Massachusetts.

In 1898 he offered his service to the Government for the war with Spain. The offer was accepted, and he was commissioned Contract Surgeon U. S. Army on August 22, 1898, and was ordered by Surgeon General George M. Sternberg, to Puerto Rico as Sanitary Inspector attached to the staff of Gen. Guy V. Henry. On March 19, 1899, he was commissioned Major and Brigade Surgeon, U. S. Volunteers, and was mustered out on June 30, 1899.)

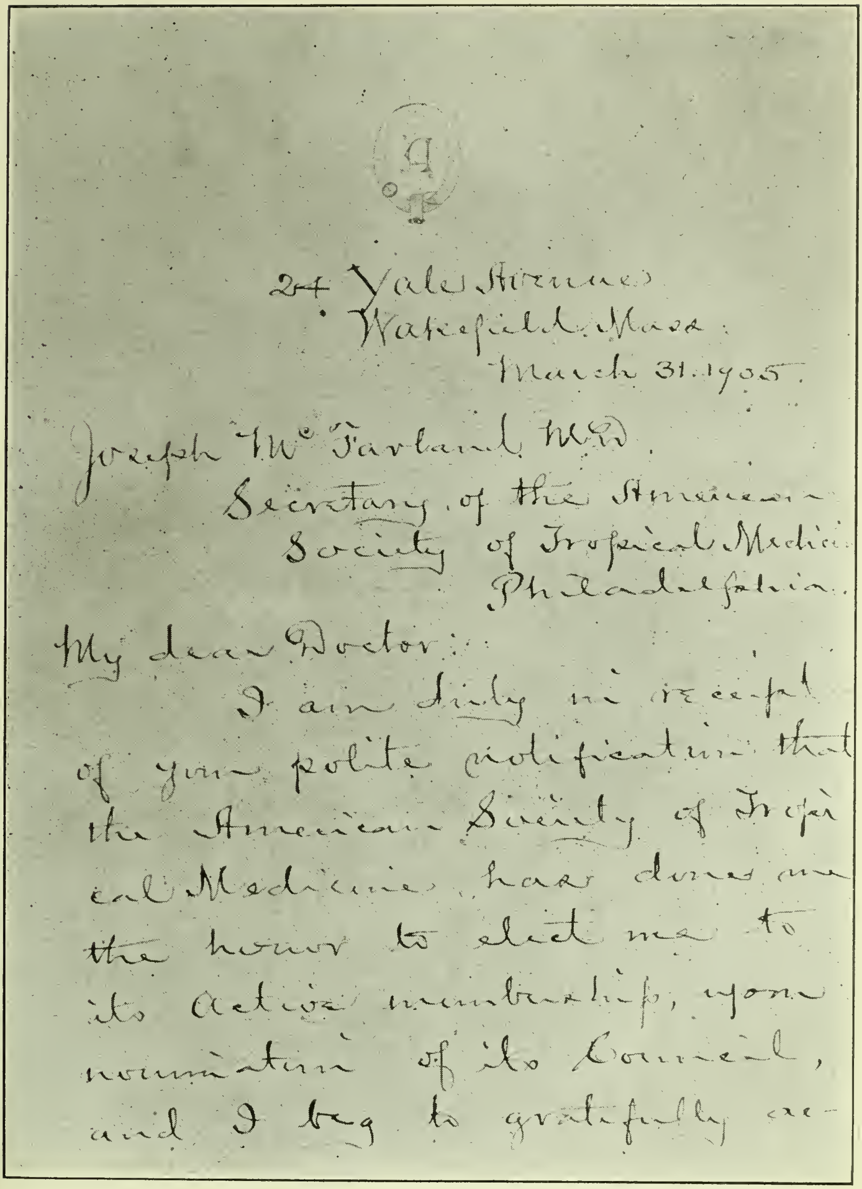
The most important work done by Dr. Ames is probably that represented in his paper entitled "The Vaccination of Porto Rico; A Lesson to the World," read before the Association of Military Surgeons in 1903, and published in the Journal of the Association of Military Surgeons the same year. In October, 1898, an epidemic of smallpox began in Puerto Rico, which by February, 1899, had extended until there were at least 3,000 recent cases of the disease in the island and the infection was still on the increase. Dr. Ames was authorized by General Henry, through the influence of the Chief Surgeon, Col. John Van R. Hoff, to start a farm for the production of vaccine virus in the island. It was understood, however, that the project should be a civil one, conducted through and in co-operation with the Alcaldes though having all possible assistance from the Army. Systematic compulsory vaccination was begun in February and was prosecuted until July 1. During that time 860,000 vaccinations were done in a population of 960,000. Of these 87.5 per cent were successful. The work then ceased because it was completed, the disease having disappeared. At the time of publication of Dr. Ames' paper the death rate from smallpox in Puerto Rico had fallen from 621 to 2 per annum. Here is a set of figures, which may in the future be used by American authors, as good as the classic figures derived from the experience in the

German Army, so frequently quoted by statistical writers. The establishment of a vaccine farm and its hygienic management in a temperate climate is no mean task. If one stops to consider the detail work necessary for the production of enough vaccine to do 860,000 vaccinations in four months, starting with nothing, the magnitude of this accomplishment and its significance may be appreciated. When, in addition, one remembers that the work was done in the tropics, where tuberculosis, glanders, actinomycosis, and the screw worm flourish, and with the assistance of many subordinates entirely inexperienced in the work to be done, the result speaks for the character of the man who, by his diligence, earnestness, and capability, achieved it.

Twelve hundred and forty head of young cattle were used; the initial lymph, the ivory points, and the apparatus necessary for the operation of the farm were obtained from a distance of 1,800 miles; a corps of over one hundred men was organized and subsisted; and the whole outfit was managed so that 16,200 points were made every day, of which 15,000 were issued to the force doing the actual vaccinating. General J. C. Breckenridge, Inspector General of the U. S. Army, wrote of the work of the vaccine farm, "It seems one of the best energized and organized, and, despite the considerable difficulties, the most successful and thorough undertaking that has characterized the American occupation."

Upon going over the correspondence of the Secretary's office, which was turned over to me by Dr. McFarland, the former secretary, when I assumed the duties of secretary of this society, I came across some letters from Dr. Ames. The clear, legible, precise chirography struck me as that of a man who would be prompt and conscientious in the performance of his duties, who would have clear ideas readily expressed upon subjects with which he was familiar, and who would by attention to detail bring success to a project that might fail in other hands.

Genealogy and colonial history were Dr. Ames' hobbies. He was the author of "The Mayflower and Her Log," published by Houghton, Mifflin & Co., in 1901, and of "The History of the Ames Family in America." In this connection he was a member

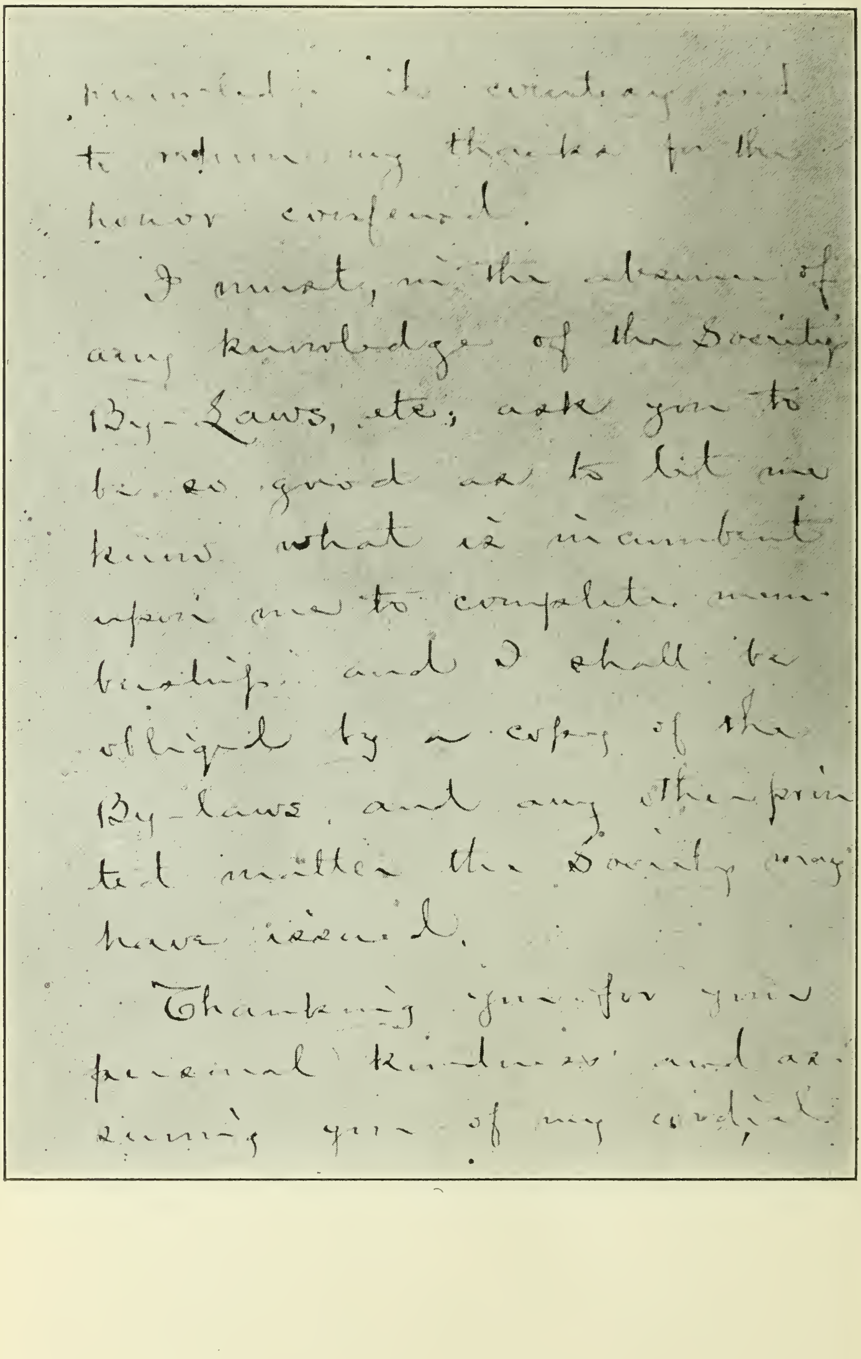


24 Yale Avenue
Wakefield, Mass.
March 31. 1905.

Joseph Mc Farland, M.D.
Secretary of the American
Society of Tropical Medicine
Philadelphia.

My dear Doctor:

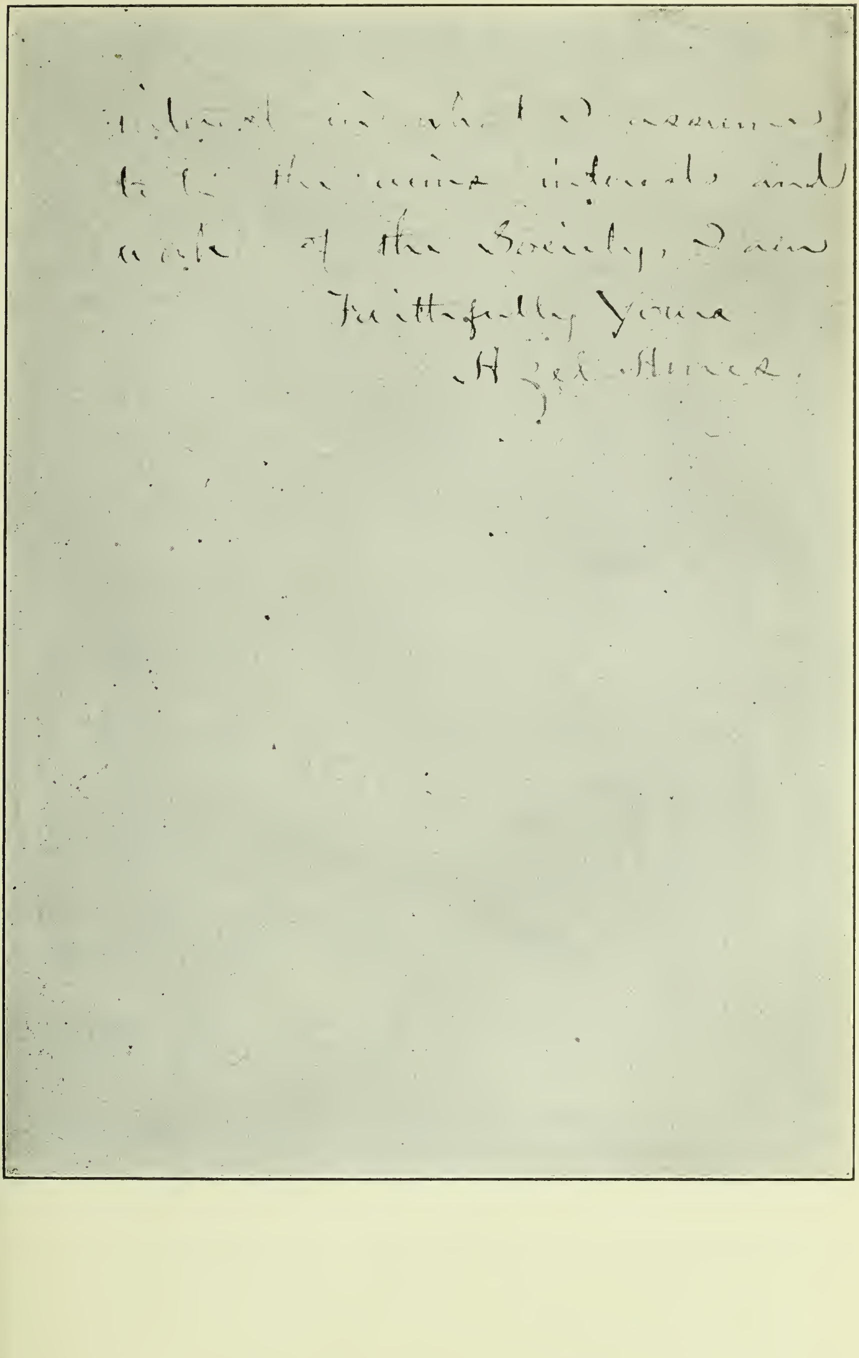
I am duly in receipt of your polite notification that the American Society of Tropical Medicine has done me the honour to elect me to its Active membership, upon nomination of its Council, and I beg to gratefully ac-



present in the evening and to return my thanks for the honor conferred.

I must, in the absence of any knowledge of the Society's By-Laws, etc., ask you to be so good as to let me know what is incumbent upon me to complete membership; and I shall be obliged by a copy of the By-laws, and any other printed matter the Society may have issued.

Thanking you for your personal kindness and assuring you of my cordial



interested in what I assume
to be the same interests and
work of the Society, I am
Faithfully Yours
Azel Ames.

of the Pilgrim Society, the New England Historical Genealogical Society, and the American Historical Society.

Dr. Ames did not contribute to the proceedings of this society, to which he was elected on March 24, 1905, at one of the Philadelphia meetings. Upon his return from Puerto Rico, Mrs. Ames noticed that the exacting and laborious task accomplished in that island had again undermined his health. In 1907 he failed markedly both in physical and mental health. He was soon discovered to have chronic nephritis and after a progressively downward course the disease ended fatally on November 12, 1908.

Dr. Ames was a member of the East Middlesex County Medical Society, of which he had been in his younger days secretary and president. He was also a member of the Medical Society of the State of Massachusetts and of the American Medical Association; the American Public Health Association, of which he was the secretary for three years; the Association of Military Surgeons of the United States, as well as a number of organizations open to those who had taken part in the Civil War.

In addition to the works already mentioned Dr. Ames was the author of the following books and essays:

A lecture before the Lansing Scientific Association, December, 1877.

The Work of Local Boards of Health. Boston, Wright & Potter, 1874.

Sex and Industry; A Plea for the Working Girl. Boston, J. R. Osgood & Co., 1875.

The Meat Food Supply of the Nation and Its Future. Tr. Am. Pub. Health Ass., 1887.

The Sanitary Condition of Working People.

Elementary Hygiene for the Tropics, 1902. D. C. Heath & Co., Boston.

The Family and Vicissitudes of John Phillips, senior, of Duxbury and Marshfield; 1903. Press of G. E. Dunbar, Malden, Mass.

A Medical Reserve Corps for the United States Army; 1905. Cornman Printing Co., Carlisle, Pa.

AN AMERICAN SCHOOL OF TROPICAL MEDICINE.*

By ISAAC WILLIAMS BREWER, M.D.,

FORT WARREN, MASS.

WHETHER we approve or not, the United States has expanded, and become a colonial nation, assuming all the complexities of tropical administration. Not the least of these new problems that have come to the nation, are those relating to the sanitary administration of our new possessions, and upon their solution depends in a large measure the outcome of our tropical ventures. These problems must be met and solved by American physicians working in the tropics in conjunction with native physicians. The men who are to do this work must be carefully instructed in the many duties they will have to perform. Sir Patrick Manson spoke very feelingly upon this subject in his Lane lectures,[1] saying: "To send a young fellow fresh from the schools to some tropical and unhealthy climate to treat diseases he has never seen before, many of which he has never heard of before, is not only cruelty to the doctor, but it may be death to the patient and bad business all around. A merchant would not think of running his business on such lines. Why, then, should the

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*Read by title at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, April 10, 1909.

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medical business, the most important of all business, in that it deals with human life, be run on such lines? I could cite hundreds of instances in illustration of the folly, I might also say the criminality, of the old system, by which raw, untaught and inexperienced youths were launched in the tropical service. Many of these illustrations, I am sorry to have to say, would be culled from the long category of my personal mistakes."

Doctor F. C. Wellman[2] who has spent many years in tropical Africa says: "The successful settlement of the tropics is of the greatest importance to the world. Such settlement depends in no small measure on the solution of various hygienic and epidemiological problems there obtaining. In the absence of this knowledge an extra expenditure of lives and money is certain to ensue. The problems in question can best be studied by trained observers working at first hand, in other words, by scientific men living in the tropics. With these points before us there is no occasion for me to dwell on the necessity for adequately equipped pathologists, clinicians and sanitarians, especially trained in the lines along which their investigations will run, to take up the enormous task awaiting them. It is no less than a cardinal sin to send poorly equipped men to the tropics."

Doctor George Dock[3] of New Orleans says: "Another pressing need is more extensive activity in the investigation of tropical diseases in the United States. I would not for a moment minimize the splendid advances made by private individuals, as well as by various departments of the government, but the field is unlimited and includes the diseases of all lower animals as well as man. The valuable results of the schools of Tropical Medicine of Liverpool, London and Hamburg show what may be done and what should be done by all countries having similar problems."

The physician who goes to the tropics to practice finds his duties very different from what they would have been had he remained at home, and the maxims taught by preceptors do not seem to apply to the conditions under which he is living. He is confronted by a host of strange diseases. The irruptive fevers which occupy so much attention at home are less prevalent, while malaria, and diseases of the alimentary canal are very common. Skin diseases, of which many practitioners in this country know very little, are prevalent and perplexing. The microscope is to be his daily companion and there are but few accommodating laboratories where such work can be done for the asking. The examination of the stools must be a routine. The study of the mosquitoes, both in the adult and the larval stages, will occupy much time, and the superintendence of the abolition of their breeding places will require tact and good judgment. This is really the work of the engineer, but there will be no engineer and the doctor will have to fill his place. There are a host of undetermined fevers in the tropics which must be studied with care before any progress towards their prevention can be made. The inspection of food, a subject which is practically untaught in our schools, must be a daily duty. In fact, in addition to the ordinary work of a physician or surgeon, the practitioner in the tropics will have to fill all the positions on the board of health from sanitary engineer to food and meat inspector. Besides he must be a medical zoologist, a bacteriologist and a diplomat.

Have the graduates of our medical schools been sufficiently instructed in all of these specialties? We may safely answer no!

Recent inquiry of the leading medical schools in this country has shown that although they all recognize the importance of instruction in tropical medicine there is no place in the United States where such instruction can be had. Doctor John M. Swan has established a laboratory course in tropical medicine at the Philadelphia Polyclinic, but he informs me that the instruction given does not include clinical teaching, and it is doubted very much whether satisfactory results can be obtained without bedside teaching.

Medical zoology occupies a small place in the course at medical schools in this country. In the Philippines this is probably the most important branch of medicine. I have more than once seen good practitioners who on their arrival there were entirely unacquainted with the amoeba or the intestinal parasites.

Hygiene, although occupying much of the attention of the public, is practically untaught in most of our medical schools. Yet in the tropics every physician has to be well posted in this branch of medicine.

The days when a physician isolated from contact with his fellows could by hard work and careful observation become a good and useful practitioner of medicine are passing away. The progress of medical science is so rapid that a few years of isolation puts a man behind. Especially is this true in the realm of tropical medicine where there are so many new discoveries in etiology and treatment.

If we are to obtain the best results from the men who are to represent our country in the tropics we must provide some means whereby they may become reasonably proficient in their many duties before they leave this country. Most of the colonial countries of Europe have recognized this and have provided schools where such instruction can be obtained. The London School, the oldest of these, has been in existence for about ten years and has had something like seven hundred students. Many of the graduates are now filling posts of importance in the tropics, while not a few have added materially to the world's stock of knowledge. This last is especially true of the Liverpool School, which has sufficient funds to provide for commissions to study the diseases of the tropics in the endemic areas.

Our laboratory workers and sanitarians in the tropics have accomplished much of which the nation is justly proud, but there is so much to be done that we should do all we can to obtain facilities for training men to continue the work which has begun so brilliantly.

The work so far has been mostly done under the auspices of the government, but it is well known that our legislators are averse to making appropriations unless they bring immediate returns, therefore there will come a time when this work will be abandoned by the government, and we should therefore provide an institution to continue this important work, an institute for the study of diseases peculiar to the warmer regions of the globe. There should be attached to this institution a well-appointed hospital and a school for the instruction of physicians in tropical medicine and hygiene. It should have sufficient funds to send experts to study the diseases in their endemic areas. The institute should be closely affiliated with the laboratories in Manila, Porto Rico, the Canal Zone, and Hawaii, and should make arrangements for an exchange of workers so as to advance the work as much as possible. Practitioners in the tropics should be encouraged to send there pathological and other interesting specimens, which should be kept and made available for study by those interested in the subject. This institute should be the "home office" of the tropical practitioner and a gathering place for all interested in the advancement of medicine in the tropics.

The services of the trained specialists of the institute should be at the disposal of the government whenever needed. They should also aid the workers in the tropics with their experience and advice as much as possible.

The study of the so-called tropical diseases is not only of importance to those who dwell near the equator, but also to the entire world. Many of these diseases are only relatively tropical. Within the past few years several of these diseases have been found to prevail extensively in the warmer portions of the United States.

Our ignorance concerning conditions in the tropics is appalling. We know nothing of the proper diet for the white race in such regions. There are those who believe one should live as the natives do and abstain from meats, while others say the beef ration should be liberal. One student of tropical medicine tells us that the cause of the decay of the white race in the tropics is the intense light. He also advocates the liberal use of alcoholic stimulants. Others of long tropical residence deny these premises. These points and many others should be determined scientifically, for if we are causing disease amongst our countrymen who are working in the tropics by overfeeding them or by exposing them to the intense light the sooner we know it the better.

There are no doubt many men who could furnish the funds for such an institute if they were aware of the importance of the work to be done. It has been estimated that $500,000 will provide for the school, and as much more would make a good foundation for the other work. Once the foundation is laid smaller sums will be forthcoming to provide for special work.

During the last few years there have appeared a number of papers advocating the establishment of an American School of Tropical Medicine. Most of these have boomed some city as the most desirable location for the school. This has done good by keeping the question alive, but it does not seem wise at this time to expend our energy discussing the merits or demerits of any city, but rather to make a united effort to secure the funds for the foundation of the Institute, leaving the question of location to a committee of physicians as was done in locating the Rockefeller Institute. The important points to consider in choosing a location are the supply of clinical and laboratory material and the convenience of the students.

REFERENCES.

1. "Lane Lectures on Tropical Medicine," 1905, p. 225.
2. *New York Medical Journal,* August 4, 1906.
3. "Tropical Diseases and the Mississippi Valley," p. 6.

Reprinted from the New York Medical Journal for July 24, 1909.

THE TEACHING OF TROPICAL MEDICINE OUTSIDE OF THE TROPICS.*

By E. R. Stitt, M. D.,
Washington, D. C.,

Surgeon, U. S. Navy; Instructor in Tropical Medicine, U. S. Naval Medical School; Lecturer on Tropical Medicine, Jefferson Medical College.

(*Published under the Imprimatur of the American Society of Tropical Medicine.*)

A few years ago it was my good fortune to be advised by Professor Welch as to an advantageous course of work for one to pursue who desired to prepare himself for medical work in the tropics; which, expressed in a few words, was to acquire a practical grasp of the problems of clinical bacteriology and to obtain a working knowledge of animal parasitology—the clinical experience to be gained later in the tropics.

The value of such advice must be apparent to those who have been in the tropics where the practitioner versed in laboratory technique not only has a local reputation superior to that of the purely bedside diagnostician but in addition, as regards an international reputation, has the advantage entirely in his favor.

Before outlining the course which appears to me advisable for one to pursue in the study of tropical diseases it would seem best to bring out certain considerations which bear distinctly on the subject under discussion. In the first place it must

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be recognized that the majority of diseases common to tropical pathology are more or less common to temperate climates, with this distinction, however, that they tend to show anomalous features. Again, that the overshadowing trio, tuberculosis, syphilis, and typhoid fever, must there be kept in mind even more prominently than in temperate climates where there are fewer similar diseases to cause confusion.

The most conspicuous feature of tropical pathology is the great incidence of diseases due to animal parasites. These are favored, not only by reason of less inimical temperature environment for the particular parasite, but also because in the tropics insect life flourishes and the opportunities for the transmission of diseases requiring intermediary hosts are greater. As regards bacterial diseases it would seem that the more favorable conditions for the growth of saprophytes should be distinctly of importance in checking the development of the more delicate pathogenic organisms. The greater importance of bacterial diseases in the tropics must, therefore, be a matter of neglect of hygienic principles rather than of a favoring climatic environment.

The work of Strong, Musgrave, and Clegg in the Philippines has shown that symbiosis is a factor to be taken into account in the production of pathogenic manifestations; now, is it not reasonable to conjecture that many of the unexplained phenomena of various diseases are due to this matter of association between animal parasites and bacteria—the resulting clinical signs differing from those usually recognized as belonging to the uncomplicated bacterial or animal parasite infection. With these general considerations in mind it would seem advisable to treat the subject of a suitable course in tropical medicine, when such a course is not given in the tropics, under three general heads: 1, laboratory instruction; 2, clinical teaching; and 3, didactic lectures.

Laboratory Instruction. — This should embrace practical work in bacteriology, pathology, animal parasitology, and chemistry. In bacteriology the training should be in the direction of having the student become familiar with the normal bacterial flora of the parts of the body and the excretions and secretions usually studied in disease. The smearing of agar or glycerin agar plates with the material to be examined gives only superficial colonies which can be easily studied and isolated in pure culture without the confusion due to deep colonies, as is the case with poured plates. To those who have not done much work of this kind the limited number and the constant appearance of certain species from material from nose, throat, fæces, pus, skin, etc., is very striking. If the student is familiar with normal findings the abnormal ones give little trouble.

In culturing fæces it is advisable to make use of some special plating medium. Of these lactose litmus agar is very stisfactory and easily prepared or, with a little experience, that of Endo. Both of these media aid in the isolation of colonies by their giving variation in color. The brilliant green medium of Conradi, so useful in the isolation of typhoid colonies, will probably be found of great value in tropical work by reason of its restraining power over cocci and colon bacilli.

It is very important that the making of media be taught in a practical way and, while the methods for making media as prescribed for water analysis are unnecessarily exact, yet, in one respect, equal care is necessary in clinical bacteriology—that is, in adjusting the reaction of media. Experience with students has taught me that variation from optimum reaction is often the basis of failure in culturing bacteria. The use of litmus milk and the simple Durham fermentation tube with glucose and lactose bouillon are of the greatest practical value in determinative bacteriology. Familiarity with the Gram method of staining and the use of the hanging drop preparation should be demanded. Now that animals can be easily immunized and kept at hand to furnish immune sera and when equally easily obtainable are dried immune sera perfect familiarity with the technique of both macroscopical and microscopical methods of agglutination should be required of the student. With a little practice the necessary technique is easily obtained.

With a coccus we can practically gain sufficient information from the smear direct from the material, stained by Gram, followed by culturing on agar or some special serum medium and dispense with the more elaborate outlay of media so necessary for the differentiation of the nonspore bearing bacilli. Hæmolytic characteristics and carbohydrate fermentations in the differentiation of cocci are of questionable practical value. Differentiation by gelatin liquefaction is of great value, but difficult of application in the tropics. Bacteriology should appeal to the student as a real factor in diagnosis and not as something more or less theoretical. It were better to simply isolate and become familiar with a streptococcus plated out from the nasal mucus and a colon bacillus from the fæces than to run through fifty organisms in pure culture on a monotonous succession of media.

In pathology the training should start with the proper methods of making and staining blood smears. It is astonishing the frequency with which men presumably well trained fail in this respect. The matter of artefacts and unusual appearances is sufficiently frequent in good preparations and in poor preparations is a frequent explanation of the preliminary note which is not followed by succeeding reports. Differential counts are of great value in tropical work, and differentiation of the normal and pathological blood cells should be thoroughly taught. The differentiation of the large mononuclear and transitional (the macrophages of Metchnikoff) from the large lymphocyte may not be of peculiar value outside the tropics, but when malaria, trypanosomiasis, and amœbiasis are involved such differentiation furnishes a useful diagnostic point. Romanowsky's method of staining is an absolute necessity in tropical work, and checked by the reliable hæmotoxylin and eosin staining gives one adequate means for the study of blood films. Where malarial cases are not at hand to furnish smears for the study of chromatin staining, which, however, are satisfactorily replaced by specimens sent from the tropics, the blood of rats showing *Trypanosoma Lewisi* answers well. This infection is very easy to keep up in the laboratory. As more closely resembling malaria an infection with halteridium is a good substitute—more nearly resembling malaria, however, is proteosoma, which infection is easily kept going in canaries. The infection with *Spirochæta Duttoni* is also easy to keep up in a laboratory. Fresh blood preparations are of great importance, but more calculated to lead to errors of observation than stained films. The blood in malarial, trypanosome, and spirochæta infections should be especially studied with fresh specimens. With spirochætæ the dark ground illumination is a desideratum. It is an easy matter to study amœbæ, ciliates, and intestinal flagellates by means of cultures, but amœbic and flagellate infections are now so common since our occupation of the Philippines that the more satisfactory material from a case can be readily obtained. The student should be taught some simple method of preparing tissues for paraffin imbedding. By affixing sections to cover glasses or slides these may be easily stained in various ways. In the tropics one should be prepared to stain sections not only with hæmotoxylin and eosin, but with thionin, Gram's method, acid fast staining, and Van Giesen's stain. The staining methods of Wright and Giemsa give good results. Now that certain flagellates are of such importance we should understand Levaditi's method.

In animal parasitology training in recognizing intestinal ova is easily accomplished by having formalinized fæces sent from tropical countries. The ova found in the fæces of various animals, especially the dog, cat, and rat, however, provide teaching material which is almost similar. The method of teaching animal parasitology in our laboratory as introduced by Dr. Stiles gives training only inferior to that obtained at human autopsies in the tropics. Dogs and cats after being killed at the municipal pound are autopsied and the parasites studied in the fresh state. The most prolific animal in interesting parasites is the rat. At such an autopsy we are not only able to study the infesting fleas, intestinal parasites, and embryos of trichinella but as well to learn the appearance of the normal rat so that a plague rat would be recognized by the subcutaneous injection, mottled liver, infiltrated neck glands, and pleural effusion. Fleas, bedbugs, and lice are best studied by keeping them in a test tube until the contents of the alimentary canal have been evacuated, and then to drop them into hot seventy per cent. alcohol. They are then transferred to acetone and afterward to xylol and then mounted in balsam. The generic and species characteristics can then be satisfactorily studied. For ticks it is best to give a preliminary treatment with caustic potash solution before proceeding as stated. For the study of mosquitoes it is best to collect larvæ from the pools, and place them in large aquarium jars covered with gauze. The insects can then be observed and either studied or dissected after they emerge from the pupal state. It is astonishing in how short a time students are able to distinguish larval characteristics. The architecture of mental plates and the syphonic variations are so much easier to recognize than scale characteristics, that it is a satisfaction to demonstrate larvæ to a class.

In the English schools of tropical medicine the chemical side of the laboratory work is less dealt with than the animal parasitology and bacteriological phases. In my opinion, with the development of simple methods for determining nitrogen eliminated as ammonia, of bile pigments, etc., and especially of reactions of the nature of the Cammidge reaction, many valuable diagnostic aids may be obtained. More expeditious methods of determining the digestive functions by microscopical examination of the fæces are more or less at the disposal of one trained in the microscopical appearances of fæces. Schmidt's fermentation apparatus for determining errors in carbohydrate digestion is a method which should prove of value in the intestinal derangements of the tropics.

A feature of laboratory instruction, considered by our students as of peculiar value, is the holding of frequent examinations in microscopical diagnosis. With a series of microscopical preparations, embracing ova of parasites, various intestinal parasites, important insects and arachnids, stained blood smears, pathological sections, bacterial preparations, and various artefacts, we have material to make one exercise common sense. The consideration of micrometry and the question of the limitations of the findings in certain material make one exercise judgment. The papers with the written diagnoses are handed in—the errors in nomenclature or terminology corrected, and a brief talk given as to justifiable and inexcusable errors in diagnosis.

CLINICAL TEACHING.

The idea prevails generally that ward class work is only practicable in the tropics or in such hospitals as the Seaman's Hospital in London or the one in Hamburg where many cases of tropical disease, among the sailors of the steamship lines going to the tropics, are treated. While it is undoubtedly an advantage to have a class study an actual case of a tropical disease yet, if such cases are not at hand, the lack of such facilities may in great part be compensated for by studying cases common to the temperate climates which are intimately connected with the differential diagnosis of the tropical disease in question.

A case of alcoholic neuritis when studied from the standpoint of the points of difference between it and dry beriberi will give the student almost as much information as the going over of an actual case of beriberi. A case of acute nephritis, when gone over from the standpoint of differential diagnosis, is only little less instructive than where the case is really one of wet beriberi. Various conditions giving enlarged livers can be used in clinics on liver abscess —large spleens to bring out the points of differential diagnosis in connection with kala azar. Various tuberculous troubles may resemble Malta fever or quotidian types of malaria. A case of venereal adenitis may serve for a plague clinic, and in the various lesions of syphilis we have clinical material to utilize in bringing out the differential diagnostic points between the various tropical infectious granulomata and those of this widespread infection. A case of ptomaine poisoning gives a perfect picture of a mild case of cholera. When we consider that cases of dengue are frequently sent to hospitals by those unacquainted with the disease with diagnoses of influenza, measles, scarlet fever, etc., it will be readily understood that cases with which to demonstrate the clinical picture of dengue are not lacking in the cities of the United States. A case of heat stroke has striking points of resemblance to certain cerebral types of pernicious malaria. In our Southern cities many of the tropical diseases, as dengue, uncinariasis, and malaria may be utilized directly.

Didactic Lectures.

In didactic lectures great stress should be attached to questions of geographical distribution and epidemiology. As with clinical teaching so in the lectures should points of resemblance of a tropical affection to some ordinary disease be brought out in contrast. Again, instead of detailing innumerable symptoms, the majority of which will more or less answer for any of a number of indispositions or diseases, it would seem advisable to pick out the five or six most characteristic features in the disease to serve as a solid framework for the students' conception of the disease. Let a student fix in his mind the sudden febrile onset, the anxious countenance, shortly followed by a clouding of consciousness and thickness of speech similar to that of a drunken man, with the appearance on the second or third day of exquisitely tender lymphatic glands, and he has a picture of plague much more than if the hundred and one various minor features of the disease were detailed out to him in monotonous succession. While the epidiascope and projection apparatus are invaluable in lecturing yet there are such things as word pictures. Bring out the fact of a mouth so sore that the lightest wine burns like brandy, then touch on the ulcerations of the mouth, the burning in the gullet on swallowing, the gastric and intestinal distress, and finally picture the repeated replenishing of the bed pan with a copious, putty colored, pultaceous, fermenting mass of fæcal matter, and the most inattentive student grasps the essential features of sprue. Present to the class a picture of a disease commencing with an erythema of skin surfaces exposed to the sun, gradually going on to an ichthyotic condition, of a spruelike condition, and finally of one partaking of the characteristics of a melancholic general paresis, and we have given a conception of the disease pellagra. It is a matter of the greatest importance in lecturing on diseases which, to the one who has not been in the tropics, appear to have rather an abstract value, to bring out amusing incidents or ludicrous contrasts. In lecturing to the class on Malta fever I referred to a conversation I had with Sir Patrick Manson in 1905 relative to a number of cases of this disease which had appeared in 1894 on the U. S. S. *Chicago*. The discovery of the probable cause in goats' milk had just been announced, and Sir Patrick assured me that if we had looked into the matter of ætiology carefully we should probably have found that goats' milk was at the bottom of the outbreak. It was only necessary to suggest to the class the utter improbability of a lot of sailor men going ashore, in a European seaport, to revel in goats' milk, to thereby ineradicably fix in their minds the most important point in the epidemiology of Malta fever.

That this outline of a course in tropical medicine is entirely practicable is shown by the fact that it represents almost in detail the course in tropical medicine given at the United States Naval Medical School. In the work connected with bacteriology and animal parasitology it is certainly as thorough as that given at the London School of Tropical Medicine. In a recent article on the need for a school of tropical medicine in the United States (*Journal of the American Medical Association,* April 3, 1909, Tobey, Need for a School of Tropical Medicine in the United States) the statement was made that the taking of the course at the London School of Tropical Medicine by surgeons of the army and navy of the United States was because tropical medicine was "not taught in this country with that particularity needed for success." While agreeing with the author in other respects I should prefer to assign as the reasons for the taking of the course at the London School of Tropical Medicine the desire to take advantage of the teaching of that leader in tropical medicine, Sir Patrick Manson, and of the clinical material at the Seaman's Hospital, rather than to those given in the article.

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THE CLINICAL SIDE OF DISEASE IN THE PHILIPPINE ISLANDS.*

By THOMAS W. JACKSON, M.D.,

MANILA, P. I.

MEDICAL RESERVE CORPS, UNITED STATES ARMY.

I HAVE been much impressed during the past few years by the wealth of clinical opportunity that exists for men actively engaged in professional practice in the Philippines. Not alone is the amount of material for clinical study very great, but the distribution is very general and the variety is certainly extensive. Doubtless, in our search for the unusual things, in our consideration of the various problems of medical and sanitary administration and our pursuit of disease organisms in the laboratory, we pass by many cases of great clinical interest, which in less opulent fields of medical work would be eagerly sought and utilized for instruction purposes. While the hospitals and the medical school are doing this for the medical student we should make greater use of this material for our personal and individual improvement. In Manila, the San Lazaro, Bilibid, Civil, University, San Juan de Dios and Military hospitals afford an opportunity for most valuable post-graduate instruction. In

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provincial regions the material is less easily accessible, but there is no community in the archipelago where the establishment of a modest dispensary would not reveal a valuable amount of material for self-instruction. Such work would not only be helpful to the observer, but special diseases would be of great statistical value.

For my own part, I regret the waste of the clinical opportunity about me quite as keenly as I appreciate the cases which I have been permittted to see and study. During the past two years I recall having seen or treated the following tropical and general diseases and doubtless this list is not complete. Many, but not all, of these cases have occurred in military organizations, and the outside field must certainly be even richer. As my memory serves me I have seen cholera, beri-beri, dengue, dysentery (amebic and specific), leprosy, malarial fever (tertian, quartan and estivo-autumnal), malarial cachexia, ankylostomiasis, filariasis, bilharziosis, tapeworm, both large and dwarf (tenia saginata and tenia nana), whip-worm and ascaris infections, trichphyton infections of sevaral varieties, erysipelas, pemphigus contagiosus, yaws, smallpox, syphilis, pneumonia, pleuritis, influenza, typhoid fever, rheumatism, cancer, tuberculosis, nephritis, aortic aneurism and various heart diseases, amebic liver abscess and hepatitis without abscess, and appendicitis. When one adds to this list gunshot wounds and fractures, major and minor surgical operations, obstetric and gynecologic cases, insanity, and organic and functional nervous diseases, and a host of gonorrheal and chancroidal cases with complications, it must be admitted that medical experience here, if anywhere, is cosmopolitan.

I desire to make a few observations, with practical bearings, resulting from this experience and from the experience of others, either verbally related or reported in print.

Typhoid Fever.—Within the past two years inquiry into the prevalence of typhoid fever has led to a modification of the belief that the disease is a rare one in the Philippine Islands. It has been found to exist among both natives and whites, and to play a part of some importance in certain localities. The Surgeon General's Report for the Army for 1908 shows that the rate of incidence for the Philippine Islands per thousand men (white troops) was practically the same as for the United States (3.50 for the Philippine Islands and 3.53 for the United States), and the latest quarterly report of vital statistics for Manila (July to September, 1908) shows that thirty-three deaths from typhoid fever, all among Filipinos, occurred during these three months. Investigations by medical officers of the army show that the disease is also prevalent among the natives of the southern islands. Various departures from the classical types have been noted, but in the cases observed by me there were no specially noteworthy differences from the disease as seen in various parts of the United States and in Cuba. In the southern islands cases were reported showing deviations, both as to type and as to delayed response to the Widal test, but the modern conception of typhoid infections is more elastic than formerly and contemplates less dogmatic views as to fever curves and symptoms, while cultural and technical factors still enter into serum diagnosis.

A closer study of our cases of continued and remittent fever, with the possibility of enteric fever in mind, is therefore appropriate under the circumstances.

Cholera.—Concerning cholera I have little to say as we are soon to have the opportunity of studying valuable reports from those actually engaged in cholera work during the recent epidemic. But I cannot refrain from quoting and indorsing the following paragraph in the Third Quarterly Report for 1908 of Acting Director of Health McLaughlin. Dr. McLaughlin says: "However, cholera may be expected in the Philippines until provision is made for thorough organization of the provincial districts under trained men, the employment of local health officers properly instructed and supervised, and the education of the people as to the cause of the infection, as to cleanly habits, and the proper disposal of feces."

Personally I am inclined to wonder whether we have not committed an error in placing our sole reliance upon the laboratory diagnosis of cholera. In the report just quoted, Dr. McLaughlin points out the fact that the interval between the January, 1908, epidemic and the reappearance of epidemic cholera in Manila in July, 1908, was bridged over by a series of cases in February, March, April, May and June, which clinically resembled the true disease, some cases proving fatal in a few days, yet negative bacteriologically, so far as the agglutination test was concerned. Few medical men in Manila doubt that these interim cases were cholera cases, negative laboratory reports to the contrary notwithstanding. In other words, cholera was present during every month. I am inclined to believe that the clinical diagnosis of cholera in these cases should be accepted and that the treatment, so far as isolation, disinfection and supervision of contacts is concerned, should be the same as in the bacteriologically proven disease, especially in the light of Manila's unfortunate experience and the difficulties which attend the fight here. I am sure that no one will interpret this view as indicating a disregard for laboratory methods and exact diagnosis. Difficulties of technique and variation of agglutinability of the organism are recognized as existing, particularly during periods of quiescence of the disease. During the active period of an epidemic, Manson's law should be remembered. He states that "it may be laid down that epidemic diarrhea with a case mortality of over fifty per cent. is cholera."

Self-deception as to the non-existence of Asiatic cholera in Manila and the provinces can only result disastrously. The official report of the Acting Director of Health for the Third Quarter, 1908, gives 673 cases of Cholera, with 458 deaths for Manila, and 17,619 cases, with 11,115 deaths from cholera for the provinces outside of Manila for the three months reported.

Dengue.—Concerning dengue, a disease which plays no part in the mortality statistics of the Philippines but figures distinctly in the morbidity among both natives and whites, there is naturally and properly much interest. This disease deserves closer attention, especially from the side of diagnosis and prophylaxis. During the past year (by reason of my station at Fort McKinley, where the disease prevails) I saw many more cases than in the previous twelve months, and I appreciate, more than ever, the difficulties attendant upon the diagnosis of the numerous sporadic cases, some of them atypical, which occur. In the midst of an epidemic the diagnosis by exclusion and by the direct method is not difficult in the great majority of cases, but in the isolated cases, constantly occurring, considerable diagnostic care is called for. As is well known the diseases which dengue most resembles in this latitude are malarial fever and influenza. From the former it may be definitely differentiated by microscopic blood examinations, but it should be remembered that a single negative blood examination is hardly sufficient to exclude malaria, as the parasites may be difficult to find under certain conditions—for example, owing to their small size immediately after sporulation or owing to their relative scarcity in the peripheral blood in certain stages of infection with estivoautumnal organisms. Three negative examinations of blood within forty-eight hours, however, will ordinarily suffice to exclude malaria.

The cases of dengue which, probably, most resemble malarial attacks are those relatively infrequent ones with single febrile periods, and the absence of the eruptive feature. A dengue case terminating its febrile course with a critical drop in temperature at the end of twenty-four or thirty-six hours will sometimes resemble malaria rather closely, but the severe pains and aches of dengue are not often simulated. The essential type of dengue, however, is a two-period fever in which the first period is sudden of onset, brief, and followed by an intermission or a marked remission; while the secondary fever is marked by a terminal rash, either distinct and striking, or faint and evanescent. This secondary period lasts for upward of forty-eight hours. The important diagnostic features of dengue, then, are the history, fever curve, pains and eruption.

In exceptional cases dengue attacks individuals infected with malaria. A puzzling symptom-complex may result under these circumstances.

The occurrence of influenza in the Philippines has not received much attention heretofore, but I am inclined to believe that cases occur, not infrequently, and that we must discriminate between this disease and dengue. The resemblance is well known and need not be dwelt upon here. I have recently seen more than a few cases which were clinically indistinguishable from influenza; marked by fever, catarrhal symptoms (expressed by coryza, pharyngitis, tracheitis, bronchitis and sinusitis), and general aching pains throughout the body. The temperature curves in these cases were certainly not those of dengue, and the catarrhal symptoms were prominent. In the United States these cases would be pronounced influenza without hesitation.

There is no good reason why influenza should not occur here, or why the influenza bacillus should not be freqnently imported into these islands, while the excess of sunlight and the universal open-air life led by the people—the two most discouraging conditions of existence for the influenza bacillus—will readily account for the absence of the disease in the epidemic form. Influenza occurs in Calcutta and elsewhere in India in December, January and February.

Without desiring to devote too much attention to dengue I would like to give a few of the conclusions reached by the Dengue Board at Fort McKinley, during 1908.*

The board, in brief, found that dengue has been present at Fort McKinley continuously since July, 1906, and that it has cut a decided figure in the sick report of the post. It confirmed the opinion that the disease is not contagious and tentatively accepted the finding of Craig and Ashburn that the disease is communicable by the mosquito *Culex fatigans.*

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*This Board was made up of army medical officers, and consisted of Drs. Boyer, Conner, Gapen, and myself.

This mosquito has been constantly present, and during many months has been present in greater numbers than any other mosquito. It also concluded that the disease is preventable, in military posts, theoretically at least, and that it is entirely practicable to reduce the number of cases to an inconsequential one by the destruction of mosquitoes. It is interesting to observe that Sir Patrick Manson, in a recent address, gave his endorsement to the view that the mosquito is the carrier of dengue, and stated that, "Given a patient with dengue, or with yellow fever, and you may inhabit the same room with him without risk of infection, if adequately protected from mosquitoes."

Individually, as clinical observers, we noted the symptoms of afflorescence of the buccal and pharyngeal mucosa, and of inguinal adenitis, or at least enlarged inguinal glands, in many cases, as well as all of the generally accepted symptoms of dengue.

In those cases in which leucocyte counts and differential white blood counts were made the total leucocytes were usually reduced and the lymphocytes were relatively increased.

In some hundreds of blood examinations of dengue patients no organisms were demonstrated other than a few malaria parasites.

Dysentery.—Concerning the clinical classification of tropical dysentery and its treatment I wish to express a few ideas only—the results of observations of this important group of diseases. I find the classification of tropical dysentery into bacillary and amebic varieties to be feasible and practical and, on the whole, quite satisfactory. Under the bacillary division I would expand the grouping to include some milder types of dysentery than the acute epidemic specific dysentery of Shiga (these subtypes due, perhaps, to variant strains of Flexner's or Shiga's organism), as we doubtless have true infections with *bacillus dysenteriae* which find expression in comparatively mild manifestations, both as to cases and as to epidemic occurrence. If the agglutination test be desired the test organism used should be grown from the stools of coincident cases, *secundem artem,* rather than from a laboratory strain of indefinite age or descent.

The occurrence of a few amebæ in the stools of acute dysentery cases does not necessarily indicate that the infection is amebic and not bacillary. While most of us are willing to admit that we are unable to distinguish between pathogenic and innocent entamebæ, and while we believe that all entamebæ in these islands should be regarded as potentially pathogenic, there is not, in my opinion, sufficient evidence to warrant us in pronouncing every case of dysentery with ameba-containing stools as one of amebic dysentery, pure and simple. On the contrary, I believe that a few amebæ may often be found, and are found, in the stools of patients with bacillary infections. And just here the clinical circumstances and aspects should be helpful. If it be remembered that bacillary dysentery is essentially an epidemic disease of acute onset, with a short incubation period and a more or less self-limited course; and that amebic dysentery usually begins as a moderate diarrhea, the stools at first being mucous in character and gradually becoming bloody, and that it is essentially chronic, with a marked tendency to relapse, there should be less confusion. It should also be remembered that fever may be absent in both diseases, although it is usually present in acute infectious dysentery of severe type.

Treatment.—In the past year or two, in Manila, there has been manifested some disposition, by a few men, to depart from the rather general agreement among Americans as to the treatment of amebic dysentery, which was reached in Manila and San Francisco and elsewhere in the United States, in the days when the military hospitals treated hundreds of cases of dysentery where they now treat tens. The empiric doctrine of "Ipecachuana for dysentery," much favored by British practitioners, has developed some exponents here. Personally, I have reviewed my opinions, formed in the old days when material for observation was most abundant and interest was keen, with a particular desire to find in ipecac the specific curative qualities claimed for it; but I confess that I have been unable to find them, and that I still believe that ipecac is not a specific for amebic dysentery. In my service in the medical wards at Fort McKinley during the past year I tried, impartially, the ipecac treatment and the local treatment, with colonic flushings and irrigations with amebacide solutions. The results were distinctly in favor of amebacide solutions. In cases treated empirically with ipecac it was necessary to resort to direct treatment, and in a few instances amebic cases previously scheduled for transfer to the United States, were able to return to duty with their organizations, instead, after a course of direct medication.

In August, 1908, while on transport, en route to the United States, I encountered an officer invalided home for amebic dysentery. He had been treated from the southern islands to Baguio over a period of months, and had submitted to an unsuccessful operation for producing an appendiceal opening through the abdominal wall for irrigation from above downwards. He had received the ipecac treatment upon several occasions, and he had also received colonic flushings, usually self-administered and without special attention to technique. He was emaciated, discouraged and disheartened, and looked forward to an early separation from the service. He was persuaded to take a course of high enemata with amebacide solutions, giving strict attention to technique to assure prolonged contact of the solution with diseased surfaces. These details include posture, adequate hydrostatic pressure, lengths of time of contact, adequate strength of solutions, and regularity. He arrived in San Francisco free from symptoms, fat, and fit for duty, and he is now performing duty in the United States. He expressed himself as being benefited as never before in treatment extending over nearly a year.

I do not claim that this man is cured, nor do I disregard the part which the sea voyage may have played in his restoration to health, but I do claim that his case exemplifies the superior efficacy of direct treatment in amebic dysentery. Unless we are willing to abandon our conception of the pathology of amebic dysentery we cannot escape the conclusion that direct treatment is the rational treatment.

Why should we treat a local condition of the colon by administering drugs by mouth, expecting a local action from them at the remote distance of twenty odd feet, any more than we should expect a local action upon the urethra, in inflammations of that structure, by mouth-administered drugs?

I do not undertake to say that ipecachuana is entirely without virtue in all cases of dysentery. Scheube states that when used in connection with calomel it is useful in catarrhal dysentery, but of little effect in gangrenous and chronic dysenteries, both of which latter cases come within the amebic or bacillary groups. Manson advocates ipecachuana in dysentery, as we are often reminded by its exponents, but he states also that it frequently fails, and that when found ineffective other drug treatment should be resorted to, mentioning the aperient sulphates, calomel and other drugs. He does not, however, disregard the local treatment of dysentery, but speaks with much praise of direct colonic treatment. Manson, however, makes no distinction between varieties, in discussing the treatment, other than division into acute and chronic cases.

Concerning the treatment of bacillary dysentery I have nothing new to offer, but I believe that, internally, magnesium sulphate, intestinal antiseptics and opium, judiciously used, constitute the best drug treatment. However, I should regard topical treatment by enemata, with the strictest attention to the technique of their administration, confinement to bed with close dietary supervision and careful stimulation as the really important part of the treatment. It is to be regretted that treatment by antidysenteric serum has not, as yet, entirely justified its promises. Our efforts along this line should be continued.

Concerning the particular medicament for local use by enemata, I am less insistent upon a given solution than I am upon the principle of treatment involved. In amebic dysentery it should be the mildest efficient amebacide, and in bacillary dysentery it should be an effective antiseptic, as slightly irritant and toxic as may be.

I believe that there is more than one useful solution for both classes of dysentery. Strong reminds us that there are protozoal causes of dysentery other than entamebæ, and accepts the common intestinal parasites, including hookworms, as occasional causes of dysentery, as well as the rarer parasites such as *Balantidium coli* and *Schistosomum japonicum*. He also recognizes a dysentery due to malaria. During the past year a few cases of balantidium dysentery have been found in the Philippines, and I observed the first recorded case of infection with *Schistosomum mansoni* for the Philippine Islands in May, 1908, in an American. There is some probability that this case was imported from Porto Rico. Bilharzia dysentery was a feature of the case.

I would like to say something of leprosy, tuberculosis, malarial infections, filariasis and beriberi, all of them diseases of great medical and economic importance in the Philippine Islands, but I have already exceeded my allowance of time. I shall close, therefore, with a single word about the last-mentioned disease.

Beriberi, in particular, is a disease which just now, by reason of its continuance among the native troops, is giving special concern to the military authorities, both on account of the increased number of ineffective soldiers which it causes, and on account of the baffling front it has presented to investigators hitherto. To some of us who are especially interested in the disease it appears that the present local tendency or disposition to explain beriberi solely by dietary circumstances, on the hypothesis that it is a food toxemia, or that it is incidental to fat starvation, to nitrogen starvation, or, as has been recently proposed by an observer in the Philippines, to an excess of nitrogen or protein food, is quite without warrant.

This controversy has gone on for years, and many of the theories now being advanced have been discarded as exploded by the best authorities long since. Sir Patrick Manson states that the favorite view that beriberi is caused by special varieties of rice, or by diseased or mouldy rice, has been disposed of effectually by experiments upon a large scale, prolonged and scrupulously conducted. Most of the European students of this question are in accord with this belief and are inclined to look upon the disease as an infection. Manson, in the past, has leaned to the view that the germ is a saprophyte, not invading the human body but residing locally in the soil or the surroundings of man, and that its toxin is inhaled, swallowed or otherwise introduced into the body. The weight of opinion, however, and the weight of presumption from analogy, and especially from prophylactic experimentation, points to an organismal infection as the probable cause of the disease, be this infection one communicated directly from man to man or intermediately by living carrier or through infected food. One thing is certain, viz., that here in the Philippine Islands, with material at hand, we have not followed a single phase of the infection theory to a reliable conclusion, either positive or negative. Some who have had the best opportunities to observe the disease have been content to speculate upon it along lines previously followed by others to logical negative endings. There remains, then, this opportunity and this duty, and unless promptly embraced the honor of discovery and the credit for the resultant benefits to mankind will not go to Americans.

It seems to me that we should be more careful in making the diagnosis of beriberi. I am inclined to doubt whether all cases so reported are true beriberi, and I freely admit that I have been puzzled more than once by some cases much resembling rudimentary beriberi, yet lacking a convincing symptom complex and history. When it is possible to diagnose beriberi at all it shoud be possible to classify it, as both the classifications of Scheube, based upon clinical expressions, and of Wright, based upon pathological expression, are comprehensive and contain ample subdivisions. Owing to the native misuse of the term beriberi and to the difficulties in eliciting true and complete histories from our native patients we will frequently be handicapped.

It has been suggested to me by a careful observer that the Filipinos, while not a drunken people, are more given to tippling than is generally supposed. He points out the fact that almost every native or Chinese tienda (store) is also a saloon for the retail sale of liquor, and that many natives, both men and women, consume considerable quantities of gin and impure native alcoholic drinks, daily and habitually. I have confirmed this observation to my own satisfaction, and consider it not improbable that many of the indefinite cases reported as beriberi are in reality, cases of alcoholic neuritis.

MANILA, P. I.

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REPORT OF THE PROCEEDINGS OF THE THIRD INTERNATIONAL SANITARY CONVENTION.*

By R. H. von Ezdorf, M. D.,
Quarantine, La.,
Passed Assistant Surgeon, United States Public Health and Marine Hospital Service.

Under the Imprimatur of the American Society of Tropical Medicine.

In compliance with a call for the assembling of the Third International Sanitary Convention of American Republics by Dr. Walter Wyman, chairman of the International Sanitary Bureau, dated June 18, 1907, the convention was held in Mexico City, December 2 to 7, 1907, to which thirteen republics sent a total of twenty-three delegates. The Bureau of American Republics also sent a representative.

The meetings were held under the presidency of Dr. Eduardo Liceaga, with Dr. Juan Jose Ulloa, as secretary. These officers had been elected at the previous convention held in Washington in 1905.

The sessions were held in a hall of the Treasury Department in the National Palace.

The provisional program which was prepared by the chairman of the International Sanitary Bureau, Dr. Walter Wyman, was as follows:

(1) "Each delegate will bring a paper relating to the nation he represents. This paper will cover the following points:

(a) A report on the existence of transmissible dis-

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eases which may prevail in its territory, especially with reference to bubonic plague, cholera, yellow fever, malaria, beriberi, and trachoma. This report will give detailed information on the measures which have been adopted for the prevention or stamping out of any of the diseases above mentioned, if they are unfortunately present in the country represented by the delegate.

(b) A report on the condition of the ports of his country, specifying the works which may have been executed therein, those in course of construction and those which are projected, as well as the manner in which the problem of water supply, of proper sewerage and of the connection of house drains with that system has been solved, as well as the methods that have been employed or are proposed for the sanitation of dwellings.

(c) A return of the assistance which the general governments may have furnished to the respective states or municipalities, for the execution of sanitation works in the cities and ports.

(d) A report on all the sanitary police laws which have been issued since October 14, 1905.

(2) Every delegate will suggest some practical means to prevent persons who may be suffering from tuberculosis from transmitting the disease to the healthy persons who may be traveling in their company either in trains or in vessels.

(3) As forming part of the order of the day, the delegates will be at liberty to present original papers relating to the following points:

(a) Studies directed to the discovery of the germ of yellow fever.

(b) Studies directed to the investigation as to whether there are other means of transmission of yellow fever and malaria besides the sting of the mosquitoes.

(c) Studies directed to the perfection of the methods of combating the mosquito.

(4) Each delegate will present a report upon the organization in his own country of the commission of three medical or sanitary officers intended to form part of the International Sanitary Commission of Information of the American republics, as provided for in paragraph 3 (b) of the resolutions adopted at Rio de Janeiro.

(5) Report upon the establishment of the Sanitary Information Bureau of Montevideo, as provided in paragraph 3 (c) and paragraph 4 of the resolutions adopted at Rio de Janeiro.

(6) Report upon the establishment of relations between the International Sanitary Bureau at Washington and the Bureau Sanitaire International of Paris, as provided in paragraph 3 (d) of the resolutions adopted at Rio de Janeiro.

(7) Besides the full papers and reports above mentioned, each delegate will bring an extract of the same, but so concise that it can be read in fifteen minutes. These extracts alone will be read during the meetings.

(8) All the extracts will be written in Spanish and English. Those presented by the delegates from Brazil will be in Portuguese and English, and those by the delegates from Haiti will be in French and English, so that while each delegate reads his extract in his own language, the others can follow, reading the same document in the language with which they are familiar."

The first session was held on the morning of December 2, 1907, at 10 o'clock, and was addressed by the vice president of the republic of Mexico. Don RAMON CORRAL. In his address he briefly summarized the work and results obtained by the previous two conventions, and pronounced the work of the present convention and all conventions to come, in formulating principles relating to public health for the adoption of all nations, a duty to civilization. The spirit of his nation, he said, was to abide by such results as had already been demonstrated by the expenditure of large sums of money and free appropriations for sanitary purposes. He welcomed the delegates to Mexico in the name of the president of the republic.

Dr. LICEAGA then welcomed the delegates. He reviewed the work of the previous conferences, stating that the first convention was a congress of hygienists, who expressed their adherence to the advanced position of sanitary science. The second reached an agreement between the nations concerning measures for defense against plague, cholera, and yellow fever. He then asked for the adoption of defensive measures against tuberculosis, malaria, beriberi, and other infectious diseases. The logical method was to prevent diseases from originating in the country itself, and that the ideal method would be to have cities provide good water supply, drainage, sewerage, paving, light, and ventilation, and to prevent the overcrowding of buildings, so that they cannot be invaded by transmissible diseases.

He then reviewed some of the work done in Mexico, particularly with regard to the eradication of yellow fever, which had existed along its Gulf coast for four centuries. The campaign waged against the epidemic in 1903, which had spread as far as the northern frontier, practically eradicated the disease in three months. The succeeding campaign to eradicate the latent foci in the states of Tamaulipas, Vera Cruz, and Yucatan, resulted in limiting the disease to five isolated cases in eleven months.

He then mentioned bubonic plague, which had been eradicated after a campaign of six months following its appearance on the Pacific coast of the republic.

He then said: "I have mentioned these examples in order to demonstrate how great is the obligation under which we all stand to attend to the sanitation of our cities; not only the great centres of population, but also the smallest ones, even the villages."

He concluded with an axiom for the guidance of all nations of America, "To defend our legitimate interests without injury to ourselves or doing injury to others."

Dr. O. GONZALES CRUZ reported for Brazil. He said that the sanitary conditions of Brazil were improving every year as the result of the campaign waged against infectious diseases. A special organization administered sanitary measures against yellow fever: (1) The isolation of those suffering from the disease and the fumigation of the houses occupied by them. (2) The systematic destruction of mosquitoes. (3) The verification of deaths and medical vigilance over persons not immune residing in the infected centre. In order to prevent the spread of bubonic plague, the extermination of rats, the destruction of fleas, the disinfection of houses, the isolation of cases, the inoculation with antipest serum was being practised. The use of serum was reported to have reduced the mortality from this disease fifty per cent. The destruction of mosquitoes in cities and the administration of five grains of quinine every three days were adopted with excellent results for the prevention of malaria. Immigrants who were suffering from trachoma were debarred. Vessels were thoroughly disinfected when beriberi had occurred.

Floating plants, completely equipped with disinfecting apparatus, were in operation at Rio de

Janeiro and Santos. Other ports, as Bahia, Para, Maranhao, Rio Grande do Sol were to be equipped with like plants.

The federal authorities contemplated forming a complete sanitary organization of all ports of Brazil. Plans were in preparation for equipping all ports with disinfecting plants and hospitals.

Dr. J. J. ULLOA reported that important port and sanitary works were in progress in Costa Rica and that the most approved modern sanitary appliances were being introduced.

No plague, yellow fever, beriberi, or trachoma has been reported.

Malaria prevailed, especially on the Atlantic and Pacific coast regions.

About 72 per cent. of the mortality in Costa Rica occurred in children under five years of age.

The sanitary state of the country with respect to yellow fever had been excellent, owing to the adoption of measures for exterminating the *stegomyia calopus.*

Dr. HUGO ROBERTS gave a detailed account of the sanitary organization of Cuba, which had a National Board of Health. The Quarantine Service enforced laws and regulations which were practically the same as those of the United States; the superior board of health or national sanitary department supervised all matters concerning public health and sanitation in the republic.

He discussed the work of the immigration service and the occurrence of yellow fever in Cuba since its reappearance in November, 1905. No plague had thus far occurred, but some observations were made with a view of determining the distance which rats would swim in Havana harbor. For this experiment six rats were thrown into the bay of Havana and their movements observed. The following observations were made:

(1) Rats are able to remain on the surface of the water for from thirty-five to forty-five minutes.

(2) They do not swim in a straight line.

(3) If they happen to see a floating object, they steer for it, seize it, if possible, and hold on unless separated from it by force.

Consequently (1) it is sufficient to anchor the vessel requiring fumigation fifty metres from shore, as rats will not cross this distance unless carried by a current or some floating object.

(2) Floats should be placed near the vessel, so that rats falling into the water may find ready refuge where they may be easily killed.

The delegates from Chile reported as follows: In Chile matters of public health are entrusted to a Department of the Interior and to the municipal governments.

Whatever public health measures are promulgated by the Department of the Interior, upon advice of the superior council of health and Institute of Hygiene, at Santiago de Chile, are enforced by the intendants, governors, and officers representing the executive in their respective territories. Bubonic plague formed seventy-five per cent. of the cases of plague observed in eight coast cities; the septicæmic or intestinal form gave five to six per cent., and the pneumonic formed one to two per cent.

No yellow fever was reported. Malaria and beriberi were unknown. There had been an extensive epidemic of smallpox. Typhoid fever was endemic.

The delegates from Ecuador reported: The Board of Health of Guayaquil, which is the principal port of Ecuador, is an independent body. It has representatives in all ports, and its jurisdiction extends over five provinces. In enforcing public health measures it has adopted and is guided by the rules laid down by the convention of Washington.

An effort will be made to have congress pass a law making vaccination compulsory.

A drainage canal is to be built in Guayaquil which will be indispensable for the sanitation of the city in the work of exterminating yellow fever and malaria, which are endemic.

In Quito, the capital city, a sanatorium for tuberculosis is about to be completed, which it is said will rival any institution of its kind in Europe or America.

Trachoma, beriberi, and bubonic plague are unknown in Ecuador. A quarantine has been established at all ports against places where plague prevails. A quarantine station was established on the island of Puna in 1903, and no expense has been spared in equipping it.

Smallpox in mild form has prevailed among persons not vaccinated, but no epidemic occurred.

For the United States, Surgeon General Walter Wyman, Public Health and Marine Hospital Service, reported on the work done by the Hygienic Laboratory of the service in matters of public health, its study of typhoid fever, milk industry, supervision of vaccine and antitoxin production, uncinariasis, and tuberculosis. He submitted reports on the progress of the work of the service in San Francisco for the eradication of plague; on the leprosarium at Molakai, in Hawaii; on the National Quarantine Service, which now has forty-three stations operating since the acquisition of the Gulf port stations; on the Foreign Quarantine Service in the Philippines; the inspection of immigrants, both at foreign ports and all domestic ports in the United States; on mosquito extermination work in Baltimore, and on the sanitary works contemplated and in progress in the cities of Mobile, Galveston, and New Orleans.

The report from Guatemala stated that in May, 1906, a code of health was promulgated, providing for all sanitary regulations and measures based on recent approved methods applicable to the conditions met in that country.

Malaria prevailed in all sea coast cities. Trachoma and beriberi were said to exist in the country. Only one case of typhus fever was reported in the first six months of 1907.

There was an institute established in the capital city for the production of animal vaccine. Vaccination was compulsory.

A Superior Board of Health had been created for the direction of matters of public health. The government contemplated the erection of sanitary stations (quarantine stations?) at Puerto Barrios on the Atlantic, and at San Jose on the Pacific coast.

Since 1900 Salvador has had a Superior Board of Health. All ports are equipped with disinfecting apparatus for marine sanitation.

Vaccination and revaccination every six years is done by the government, animal vaccine being used.

Malaria in all its forms is endemic.

Tuberculosis causes six per cent. of all deaths.

No epidemic of yellow fever has occurred in Salvador since 1900. Since that date but one case of yellow fever was confirmed and six suspicious cases reported.

On account of the financial conditions of the country, no extensive works for the sanitation of cities and water supplies could be undertaken.

Discussion of the measures of the international sanitary policy against yellow fever. Dr. LICEAGA reviewed the conditions in Mexico and spoke in favor of permitting persons arriving in good health from suspected or infected ports to land without detention. He said that in Mexico the high officials were admitted without restrictions. Suspected cases of yellow fever were allowed to land and to proceed to such places in Mexico as were known to be unfavorable for the spread of yellow fever. Suspected cases entering infectible territory would be held under observation by local authorities. So far as Mexico was concerned he did not think more stringent measures were necessary or need be applied.

Dr. GUITERAS stated that such measures as advanced by Dr. Liceaga would not be applicable to Cuba, where every portion of the country had conditions favoring the propagation of that disease.

Surgeon General WALTER WYMAN stated that in the United States we had infectible and noninfectible territory; that while the general conditions in each country forced themselves on the authorities, quarantine measures were about the same for all, and would need to be applied as the necessities arise and circumstances require. It was, therefore, not necessary to take the same measures against a vessel from an infected port in Boston as in our southern territory.

Dr. CRUZ stated that isolation was impracticable in his country, and for that reason daily inspections were made of all sick and suspects. As many as 4,000 visits were made in one day.

Discussion on malaria.—Dr. LICEAGA opened the discussion. He said that in Mexico the sanitary forces, now engaged in the work of exterminating yellow fever infection, would be employed to do similar service in the places where malaria prevailed. He proposed that all countries carry on a crusade against malaria in the same manner as was done in tuberculosis.

Dr. GUITERAS stated that the majority of persons detained at Las Animas Hospital, in Havana, on account of fever were found to be suffering chiefly with malarial fever, for which disease they were treated before being permitted to leave the hospital and enter the country. He favored a mild quarantine and introduced resolutions to that effect.

Dr. H. L. E. JOHNSON proposed that the name of diseases transmissible by mosquitoes be called "mosquito fever." That malaria be then called "anopheles fever"; yellow fever, "stegomyia fever," etc. This nomenclature, he maintained, would give the people a more accurate notion of the cause of the diseases and would facilitate the work of the sanitary authorities in enforcing preventive measures against the spread of those fevers.

Dr. ULLOA suggested the name "stegomyia mosquito fever," "anopheles mosquito fever," etc., adding the word "mosquito" to the names given by Dr. Johnson. He said that the education of the masses was the first step toward putting down any disease, and they should know the exact causes of diseases.

Dr. GUITERAS brought out the fact that in Cuba malaria was not spread solely by anopheles, but also by other species, such as the cellia. He thought that the terms were, therefore, not applicable.

Dr. CRUZ stated that in Brazil myzomyia were present.

Dr. R. H. VON EZDORF mentioned his experience at the New Orleans quarantine station during the past summer, where all persons from the tropics arriving with fever were held for observation. It was his experience that nearly all cases excepting about twenty, which were cases of typhoid fever, proved to be malarial fever, chiefly of the æstivo-autumnal type. In all cases, however, the parasite or other evidence of malaria was found and demonstrated microscopically. He also favored the detention and quarantine of cases of malarial fever when in the active stage of the disease.

Discussion on the measures of the international sanitary policy against bubonic plague and cholera.—Dr. LICEAGA gave a detailed account of the work done at Mazatlan and emphasized the following points in the campaign:

(1) Depopulation as far as possible, and notification of authorities at destination. (2) Inoculation of persons with antipest serum. (3) House to house inspection. (4) Hospital for suspected cases. (5) Lazaretto for positive cases of plague and for convalescents. (6) Observation camp for those exposed. (7) Destruction by fire of all houses which cannot be disinfected. (8) Destruction of rats, mice, and fleas. (9) Cordon about the infected town or city.

Dr. CRUZ stated that persons leaving Rio de Janeiro were vaccinated with antipest serum.

Dr. ESPIRO stated that plague had been in Montevideo in 1901; that cases had been traced to the custom house, where rat plague prevailed; that some cases were traced to bags used in packing crackers, that these bags came from Asuncion. Some cases had been traced to bags used for coffee from Rio.

Discussion on trachoma, beriberi, and other transmissible disease.—Dr. LICEAGA, in discussing the presence of some cases of trachoma and beriberi in Mexico, stated that an immigration law was in preparation providing that immigrants suffering with tuberculosis, scrofula, acute malaria, beriberi, or other transmissible diseases, be prevented from entering the country. He believed that if all nations of America adopted measures for preventing admission of immigrants sick and incapacitated for work, it would contribute materially toward the improvement of hygienic and social conditions.

Dr. HUGO ROBERTS stated that immigrants suffering with trachoma were not permitted to land in Cuba.

Dr. Ferrer, of Chile, stated that out of 17,000 known cases of various forms of conjunctivitis, only 0.14 per cent. were found to have trachoma.

Discussion on measures for preventing the transmission of tuberculosis in railroad cars and ships.—Dr. Liceaga opened the discussion on this subject and mentioned the use of metallic plates heated by electricity or other means for burning the expectoration. That on railroad cars a special place might be provided with a vessel or receiver where the passenger could go to expectorate, and where the spittle would be carried off by a current of water or destroyed *in situ* by heat. Pocket spit cups were to be used only in special cases.

Dr. Hugo Roberts, of Cuba, favored the application of prophylactic measures to vessels as well as to cities. Vessels should be looked upon as floating hotels, and frequent disinfection should be done.

Dr. Ferrer, of Chile, favored the use of envelopes for napkins when not frequently changed, to avoid contact of napkins after use.

Dr. R. H. von Ezdorf said that it was impossible to take extraordinary measures, that whatever regulations were adopted must be easy of application. The following measures were practicable:

1. Physical examination of crews before giving employment.

2. The traveling public should be educated to understand that the practice of expectorating promiscuously might be dangerous and was filthy.

3. Notices should be posted enjoining passengers not to expectorate on floors. Receptacles should be provided for this purpose. Paraffined spit cups, which were cheap, should be provided.

4. All persons should be encouraged to use individual drinking cups.

5. Living quarters of short trip vessels to be dis-

infected periodically; long trip vessels should have the steerage quarters disinfected at the end of each voyage.

6. Screening as far as practicable of the galley, dining rooms, and living quarters, to prevent the access of flies.

Dr. Soza, of Chile, recommended the following measures:

1. Avoid the use of carpets in dormitories.
2. Spittoons to be well distributed.
3. The disinfection of cars and berths.
4. The disinfection of dining rooms, envelopes for napkins when the latter are not changed frequently.
5. The examination of passengers and the isolation of suspected cases of tuberculosis.

Dr. H. L. E. Johnson, of the U. S., recommended that tuberculous subjects be not employed on cars or ships where, in the discharge of their duties, they would come in contact with passengers. That they be not employed as porters, cooks, or dining room attendants; the education of the people; the destruction of flies; separate apartments for tuberculosis subjects, and disinfection of berths and utensils.

Sanitation of ports and cities.—Dr. Liceaga presented a paper on the sanitary work done, such as providing water supply, sewerage, drainage, and paving in the principal cities of Mexico, on the assistance afforded by the federal governemnt. A total of over $45,000,000 was appropriated by the government for Tampico, Vera Cruz, Coatzacoalcos, Manzanillo, Salina Cruz, and Mexico, D. F. The amounts appropriated for the cities were in addition to sums appropriated by the states and cities themselves for carrying out the work required.

On a motion made by Dr. Espiro, of Uruguay, the delegates voted unanimously a rising congratulatory vote to Dr. Liceaga and the Mexican Board of Health in acknowledgment of the sanitary work accomplished by them.

Dr. Juan Guiteras read a paper in which he gave a history of the spread of yellow fever and the campaign made against yellow fever in Cuba since its reappearance in November, 1905.

Respecting an improvement in the methods for exterminating the mosquitoes he mentioned the plan by which large dwellings with their patios are completely covered with a tent and then fumigated. He said that this plan was working satisfactorily.

Dr. Liceaga stated that a canvas cover, in sections, is used in covering *jacals* and thatched houses to make them air tight preparatory to fumigation. The canvas sections overlapped each other when applied and the ends were fastened to the ground, so that there would be no space for a mosquito to escape.

The following resolutions were approved by the Advisory Committee and were passed by the convention:

1. The representatives of the governments of Brazil, Colombia, and of Uruguay are asked to adhere to the sanitary convention which was signed in Washington in 1905.

2. To the American governments represented in this convention is recommended the codifying of all sanitary laws and regulations of the respective countries, and as soon as this is accomplished, to forward copies of them to the International Sanitary Bureau at Washington.

3. The convention is recommended to authorize the International Sanitary Bureau of Washington to establish by means considered by them to be most convenient, corresponding relations with the international sanitary bureau of Paris, in accordance with

the declaration made by the third Pan American Congress, held in Rio de Janeiro, August, 1906.

4. That the secretary be authorized to include in the publications of the proceedings of the third international sanitary convention a summary of all the resolutions adopted by the first and second international conventions held in Washington.

5. That recommendations be made to the American governments of the convenience of agreeing upon compulsory vaccination against smallpox.

6. That recommendations be made to the governments represented in this convention of the convenience of declaring free from state taxes the salts of quinine, fine wire, mosquito netting to be used as a protection against mosquitoes, crude petroleum, mosquito bars, and material used for that purpose.

7. That recommendations be made through the medium of the respective authorities that the governments enter into a most active propaganda on the ætiology, prophylaxis, and treatment of malaria, and resolve upon the establishment of public conferences on these subjects in schools, shops, barracks, etc.

8. That recommendations be made for the establishment of centres at necessary points for the free distribution of quinine to the poor in necessary quantities for the prophylaxis of malaria.

9. That recommendations be made to the governments that they order the maritime sanitary authorities to include in the public health reports which they issue the mortality occasioned by malaria.

10. That recommendations be made to the International Sanitary Bureau at Washington that it give information to the countries represented of the existence of malaria at the principal seaports.

11. That recommendations be made to all governments alike for the publication of a pamphlet in

which is compiled in a brief, simple, and practical form, easily understood by the public, facts concerning malarial fever, for liberal distribution.

12. That recommendations be made to the governments that they prohibit the immigration of persons suffering from trachoma and beriberi.

13. That recommendations be made to the various American nations for the legal and adequate steps in favor of the nationalization and centralization of sanitary authorities.

14. That to the American governments be recommended the following suggestions for the prevention of tuberculosis in railway cars and steamships:

a. To avoid, as far as possible, the use of carpets and fixed curtains.

b. To recommend the use of spittoons well distributed.

c. Periodical disinfection of cars and staterooms, including furniture, beds, washbowls, linen, etc. These disinfections should especially be made in the third class passenger quarters. All clothing, including napkins, should be disinfected before being washed.

d. Disinfection of dining room service and the use of paper envelopes or covers for napkins used by passengers; also that food be covered with screens; that doors and windows of railroad cars, staterooms and habitations on vessels be screened with fine wire netting to avoid the introduction of flies.

e. The examination of employees of passenger trains and vessels, in order that tuberculosis subjects are not employed.

f. All vessels should have a special and comfortable department for the accommodation of tuberculosis patients, its construction not to admit of the retention of dust in any part.

g. The pasting of notices in public places condemning the habit of spitting on floors.

h. Recommending that physicians on board a vessel be not only titled in their profession, but, if possible, to have a special knowledge of the prophylaxis of tuberculosis.

15. That recommendations be made that it would be advantageous for the European nations to adopt the Sanitary Convention of Washington of 1905 for the colonies they have in America.

16. That recommendations be made to the American nations that it would be advantageous to have a uniform bill of health, and that such contain the same class of information.

17. That recommendations be made to the American governments that it would be advantageous to establish separate hospitals for the treatment of tuberculosis, and if such is not possible, then the establishment of separate wards in hospitals for the treatment of such sick.

Costa Rica was chosen as the place of the next International Sanitary Convention of American Republics, to assemble December 25, 1909.

Dr. J. J. ULLOA was elected president.

The social features included banquets, a tea at Chapultepec Café, a visit to Chapultepec Castle, where the Mexican band rendered music, a reception by President Diaz, automobile rides, and excursions.

A visit to the penitentiary proved of interest. The penitentiary occupies 32,700 square metres. Entering the administration building, the delegates were shown the administrative offices. In one room was the anthropological department, where skulls of all persons executed at this penitentiary were collected and preserved. All data concerning the individual skulls were kept on cards and a comparative study could be made with the normal skull by any one interested.

Entering the prison grounds proper, the first thing that attracted the attention was a central steel tower thirty-five metres high. This tower supported the water tanks and served as a watch tower where guards were continually on duty, and from which a perfect view was had of all parts of the prison.

The prison was said to be planned after the Irish or Crofton penitentiary system. The buildings, seven double rows of two story structures divided into cells, were built radiating from the tower.

There were two central bath houses, each built in the form of a circle, located in the prison courtyard. In the centre of each bath house was a small tower, from which a full view was had of the twenty-three individual bathrooms into which this space was divided by walls as radiating from a centre. Each individual bath or compartment was furnished with a stone wash tub, stone closet seat and closet, shower and stone bath tub.

As each prisoner entered a compartment he was locked in, and the watchmen in the tower could see that he took his bath. When the prisoners completed their baths and were ready to leave, the watchman took them through a series of setting up exercises, giving the signal and marking time for the various movements by striking a club on the rail in front of him. No prisoner could see the other, but all went through the exercises with clocklike regularity.

The water supply for the prison was from five artesian wells giving 500 litres of water per minute.

The plumbing system for sewerage and drainage was modern and of approved pattern. Toilets were flushed automatically.

The delegates were also shown the hospital, autopsy room, schools, work shops where shoes were made, carpentry and cabinet work done, palm leaf weaving, etc. Other points of interest shown were the bakery, kitchens, mess halls, steam laundry, electric lighting plant, etc.

At the disinfecting plant all disinfecting apparatus were displayed and shown by the corps of disinfectors, all of whom were uniformed. The following is a list of apparatus shown:

Formaldehyde vaporizing apparatus; vacuum apparatus, a form of hand pump and tank provided with a hose and an attachment for going over carpets, walls, etc., for taking up dust, by which process, it was stated, sixty-six per cent. of micro-organisms were removed; bichloride pump and sprays; apparatus for the safe production of hydrocyanic acid gas; a portable steam chamber; wagon, zinc lined, for bringing infected clothing to the central plant, etc.

The central plant was furnished with two chambers of the Fernand Dehaitre type, made in Paris. One was for washing and boiling clothing, the other for steam disinfection at high pressure. A partition wall completely separated the two ends of this apparatus. One room had its special entrance for receiving infected clothing to be placed into the chamber at that end. The clothing when disinfected was removed at the other end of the chamber, which opened into a room on the other side of the partition wall.

Rabies department. The laboratory rooms for the production of virus and for the treatment of hydrophobia were then shown us.

For the production of virus the first inoculation was made from a brain brought from Paris in January, 1888; animal inoculations had been made since that time. The virus caused death of the inoculated rabbit on the seventh day.

A subdural inoculation into a rabbit was made at the time of the visit; an autopsy on a rabbit which had just died was made, removing the whole spinal cord and showing the technique for making the preparations.

Since April, 1888, to November 30, 1907, the following number of persons were treated:

Persons inoculated by animals known to have rabies	518
Persons inoculated by animals probably rabitic	4,321
Persons inoculated by animals suspicious of rabies	3,457
Total	8,296

A register giving a history and other data of each individual treated was kept. There were twenty-eight persons under treatment at the time of the visit, Dcember 4, 1907.

Water supply for Mexico City. There were several sources of supply, but a new one now under construction from Xochimilco was visited.

The first point seen was the site for four reservoirs. The reservoirs were constructed of cement, with cement columns to support the cover, which was to be topped with a grass lawn.

A cement tunnel encasing a stout wire net tunnel of expanded metal would be the conduit from the source of water supply located near Xochimilco.

Sewerage system. The sewer flushing pump station was visited. A map showing the sewer mains throughout the city and their termination into the Grand Drainage Canal was explained.

The pumping station had steam and electric pumps for forcing water, 1,500 litres per second, through the sewers for the purpose of flushing them, which was made a daily service.

The sewerage system was that known as the "combined water system," comprising 1, sewers for collecting house refuse and rain water; 2, flushing pipes and pumping station; 3, main collecting sewers which discharged all waters into the Grand Drainage Canal and thence out of the valley through Tesquisquiac tunnel.

The sewer pipes were so arranged as to admit of thorough flushing, there being no blind ends where stagnant water could remain. Ventilation was provided and sewers made accessible through manholes.

The General Hospital. This hospital comprises sixty-four buildings and was constructed on the pavilion plan. Thirty-two buildings had hospital wards; seventeen were for general service, as follows: Porters' house, office of administration, residence for physicians, disinfection station, electric plant, machinery, stables and carriage house, hydrotherapeutics gymnasium and electrotherapy, operating rooms, and morgue; ten other buildings were for watchmen, and five for attendants to the various infectious wards.

There was to be a school for nurses under the direction of two German trained nurses.

Visit to the new suburbs, Juarez, Roma, and Condesa. These suburbs were real estate projects, and the plans for starting such suburb must be approved by the government. Previous to permitting the erection of any buildings, streets must be laid out and paved with asphalt, sidewalks of cement, sewer and water pipes laid, and lighting provided.

THE COMPARATIVE MORPHOLOGY OF THE SPIROCHETES OF SYPHILIS AND YAWS (FRAMBŒSIA TROPICA).*

FREDERICK F. RUSSELL, M.D.
WASHINGTON, D. C.

There has always been considerable interest in the tropical disease known as yaws or frambœsia tropica, not only for itself, but also on account of its resemblance to syphilis, and one group of English physicians, headed by Mr. Hutchinson,[1] has even gone so far as to say that if "yaws be not syphilis it is very clear that it offers a very exact parallel to it." The physicians of Mr. Hutchinson's school have tried to clear up the question of the origin of syphilis by suggesting that it is an evolutionary form of yaw.[2] All authorities unite in agreeing that the two diseases have many points of resemblance and that their relationship to one another is a most intimate one.

When the spirochete of yaws was first described by Castellani[3] in June, 1905, his announcement aroused great interest among the students of syphilis as well as among the students of tropical diseases. It seemed probable that at least one of the riddles of medicine might now be answered.

In his first publication[3] Castellani says distinctly that he does not commit himself in any way as regards the etiology of Parangi. In his second article on the subject[4] he is still non-committal. In his third report,[5] which was published only one week later, he tells us that Professor Schaudinn had kindly examined some of his preparations and had written him under date of Aug. 8, 1905, that the yaws smears contained three varieties of spirochetes, one of which was very delicate and resembled closely *Spirochæta pallida,* and at this time Castellani expresses himself very decidedly as to the identity of the two organisms. In his summary he says that one of these spirochetes is extremely delicate and, in his opinion, it is absolutely identical with *Spirochæta pallida* of

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*Read at the fifth annual meeting of the American Society of Tropical Medicine, held in Baltimore, March 28, 1908.

1. Allbutt and Rolleston: System of Medicine, Lond., 1907, ii, Part ii, 701.
2. Osler: Modern Medicine, Phil., 1908, iii, 439.
3. Castellani, Aldo: Jour. Ceylon Br. Brit. Med. Assn., 1905, ii, 54.
4. Castellani, A.: Brit. Med. Jour., Nov. 11, 1905, ii, 1280.
5. Castellani, A.: Brit. Med. Jour., Nov. 18, 1905, ii, 1330.

Schaudinn. But even after making such a positive statement as that he has apparently not convinced himself in the matter, as he adds in the same breath that "if my hypothesis should be proved to be wrong a proper name for the organism might be *Sp. pallidula.* Castellani's next article[6] is entitled "Is Yaws Syphilis?" This is not a mere note on the question, but a rather complete discussion of the entire problem, and in this paper he comes to two conclusions which at first sight are not consistent with one another. He concludes that yaws is not syphilis, and also that spirochetes of yaws are, in his opinion, morphologically identical with *Spirochæta pallida* of Schaudinn; he maintains, however, that this does not prove the identity of the two diseases, since the bacillus of leprosy and of tuberculosis and many other acid-fast bacilli are morphologically identical, while the diseases are quite distinct.

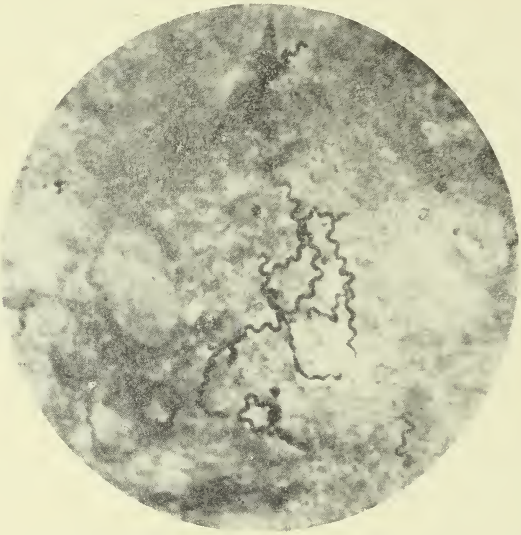

Fig. 1.—Spirochete of yaws, *Spirochæta pertenuis* (x1500).

Since 1906 three independent series of studies have been made on the subject of the unity or duality of syphilis and yaws, and the same general conclusions have been reached in all three studies (Castellani,[7] Ashburn and Craig,[8] L. Halberstaedter[9]), namely, that yaws is a separate and distinct disease from syphilis, and that an inoculation of monkeys with yaws does not confer any immunity against syphilis, nor does the inoculation of syphilis confer any immunity against yaws.

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[6] Castellani, A.: Jour. Trop. Med., 1906, ix, 4.

[7] Castellani, A.: Jour. Hyg., 1907, vii, 558.

[8] Ashburn and Craig: Philippine Jour. of Sci., Manila, 1907, ii. 441.

[9] Arb. a. d. k.: Gsndhtsamte, Berlin, 1907, xxvi, 48.

To return now to the question of the morphology of the spirochetes of these two diseases: Last summer I examined numerous smears made from yaw lesions, and I must confess that I could not satisfactorily differentiate one variety from the other, although I felt that there were certain minute differences which are too elusive, however, to be put down in so many words. Later in the year I was so fortunate as to obtain two nodules which had been excised from patients suffering with yaws; these I studied according to the silver nitrate method of Levaditi,[10] and in both specimens were found innumerable spirochetes which at first sight appeared to be absolutely identical with *Spirochæta pallida*. A little study, however, showed that there were differences between the two and that these variations were not accidental, but regular and constant. These differences may be appreciated by comparing the two accompanying photomicrographs, which were taken under exactly the same conditions as to magnification, light, etc. The photomicrographs represent average fields; they were not selected for this special purpose.

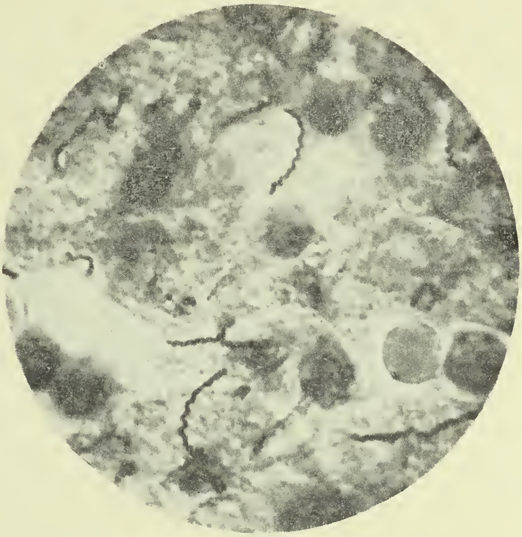

Fig. 2.—Spirochete of syphilis, *Spirochæta pallida* (x1500).

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[10] Jour. Am. Med. Assn., 1907, xlviii, 605.

It is evident: (1) That *Spirochæta pertenuis* (Fig. 1) is slightly thicker than *Spirochæta pallida* (Fig. 2).

(2) That the distance from crest to crest of the waves is greater.

(3) That the dip from the crest to the hollow is greater as a rule.

(4) That the waves are not quite so regular in their height.

(5) That the number of forms showing longitudinal division is greater.

(6) That there is a greater tendency for the spirochete to curl up one end into a loop or more or less solid ball.

Prowazek,[11] in some comparative studies on spirochetes, has come to practically the same conclusions as these. He adds one point which is of considerable interest—a point which was forecasted by Castellani in one of his earliest papers—and that is, that these organisms have a resting form which is oval or round and which is produced by a coiling up of the spiral. One often sees individuals with one end looped or coiled into a more or less solid round or oval body which represents a transition stage between the fully extended and the coiled up resting stage.

U. S. War Department.

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[11] Arb. a. d. k.: Gsndhtsamte, Berlin, 1907, xxvi, 23.

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CHICAGO:

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SCHISTOSOMIASIS (JAPONICUM) WITH SPECIAL REFERENCE TO OBSERVATIONS IN HUNAN PROVINCE, CHINA.*

BY O. T. LOGAN, MEDICAL MISSIONARY, CHANGTEH, HUNAN, CHINA.

History and geographical distribution. — For many years it has been known that a peculiar disease characterized by enlarged spleen, liver, dysentery, etc., existed in certain parts of Japan, but not until Katsurada discovered the specific cause to be a trematode, which he described [1] and named Schistosoma japonicum in 1904, was the true nature of the disease known. Catto was working on his classical case, a Chinese from the province of Fukien, who died of cholera in Singapore, synchronously and independently of Katsurada, and they published articles describing postmortem findings and the fluke that was then new to science, Katsurada's article in 1904 preceding Catto's [2] by several months.

The second Chinese case was found in June, 1905, in our hospital in northwestern Hunan, which is in south-central China, this being some twelve hundred miles from Fukien province, the home of Catto's patient. A history of this case, together with a specimen of the feces, was sent the Naval Medical School with the request that the case be published if our diagnosis was found correct. This was done by Beyer,[3] who was at that time attached to the school. Since this time we have had more than a dozen cases [4] that came from different parts of the province, and the fact that some of these patients report many of their neighbors to be suffering from a disease similar to their own makes it highly probable that schistosomiasis is not an uncommon disease in our part of China at least.

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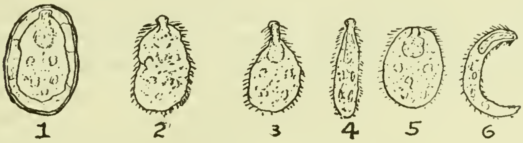
* Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the United States Naval Medical School, Washington, D. C., April 10, 1909.

In 1906 Wooley[5] reported the disease in the Philippines, Taylor[6] in Nanking, which is midway between Shanghai and Hankow, on the Yang-tse, and Booth[7] observed several cases in Hankow. Thus it is proven that the distribution of the disease is a wide one, taking in parts of Japan, central, south-central and southeastern China, and parts of the Philippines. We need not be surprised to hear that it occurs in many other locations in the Orient where wet farming is carried on, especially where people are dependent upon ponds and reservoirs for their water supply. It is not improbable that there are patients among the Chinese and Japanese in the United States at the present time who act as hosts and suffer from the effects of this fluke.

The clinical picture is extremely variable; most of our cases have had marked anasarca, but one showed extreme emaciation. Usually the liver, the spleen, or both, are enlarged, but this is not an invariable rule. Bloody stools are common, but there may be only diarrhea of varying grades. In children, the growth is retarded, as in anchylostomiasis. It should be remarked in this connection that most of our cases have had a light infection with hook worms, and this may have modified the picture somewhat.

Katsurada lays stress on the shape of the abdomen. He says, "The hypogastric region seems to shrink, while the epigastrium enlarges and a transverse furrow forms directly above the umbilicus so that the general appearance of the abdominal region is that of an inverted gourd." Studying the only photograph I possess of a case confirms Katsurada's observation except as to the transverse furrow.

Diagnosis is easy, as a rule, if the microscope is used. The characteristic ova are usually found in every specimen of feces mounted. As the presence of these eggs in the feces is dependent upon the habitat of the fluke, which never leaves the blood vessels, and also upon the ulceration necessary to allow the ova to reach the lumen of the bowel, it may be necessary to make examinations on successive days before they are found.



1. Ovum of Schistosoma japonicum in feces.
2, 3, 4, 5, 6. Shapes assumed by embryo outside the ovum.

The ova are somewhat larger than those of ascaris lumbricoides, oval in shape, colored light yellow and usually showing an embryo inside that is shaped like a melon seed. The embryo is ciliated, but the cilia are very difficult to see while the embryo is inside the shell, but when squeezed out by pressure on the cover glass, in the recent specimen, the cilia are very apparent.

Booth, of Hankow, showed me specimens from an undoubted case of Schistosoma japonicum infection in which none of the ova showed differentiated embryos. The eggs in this case were simply filled with granular material and could be recognized as eggs of the fluke under consideration only by their size, shape and color. Booth held that the dysentery the patient was suffering of hurried the eggs out of the bowel so rapidly that the embryo did not have time to develop. He had a good basis for this view as sections of tissue containing the ova never show a differentiated embryo inside the egg shell. Another explanation would be that the eggs were unfertilized.

The mode of infection is not known. Katsurada [1] believes it takes place through the skin, in people who wade through stagnant water. It is interesting to note that cats are especially prone to this disease in Japan, for this animal, I have always understood, is proverbially averse to wading. If this is the case, it would seem that infection through the alimentary tract is more likely. The only experiment on the mode of infection I know of was recorded by Tsuchiya[8] in a recent and very full article on the subject. He found that the embryo develops and breaks out of the shell when infected feces are mixed with water and kept warm. It lives several months without further development and then diminishes in size and dies. He fed such material to a dog and a cat with negative results.

Prognosis, the Japanese declare, is bad in heavy infections, and even in light infections the disease is serious because it makes the patient more liable to concurrent affections on account of his lowered resistence.

From our observations and from the reports our patients and their relatives give, I judge that the disease is to be regarded as very serious when it has developed so that symptoms are noticeable. The only two of our cases that we have been able to trace have died. It would seem that the seriousness of the disease due to Schistosoma japonicum in a given number of cases is much greater than that caused by Schistosoma hematobium.

Treatment. — Three cases have come into our hospital wards for treatment. One promptly died, another stayed only a few days, while one remained about two months. This patient improved rapidly under laxatives and iron tonics; his hemoglobin rose from 10% to 35% (Talquist) in less than a month and the dysentery, anasarca and prolapsed rectum entirely disappeared by the time he left the hospital. Although the ova were still present in the feces, the patient considered himself well. In spite of this improvement, however, we learned that he died, presumably of the disease we are considering, a few months after he returned home.

Tsuchiya [8] strongly advocates tapping the abdomen, in addition to the above treatment, when ascites is present, declaring that this condition is often cured after several repetitions of this operation.

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DERMATOBIA NOXIALIS INFECTION;

REPORT OF A CASE CONTRACTED IN SOUTHERN MEXICO.*

By JAMES D. MANGET, M.D.,

ATLANTA, GA.

J. A. M., age 38, American, resident of Atlanta. Went to Oaxaca, Mexico, in October, 1907, and enjoyed splendid health until March, 1908, when he left the city of Oaxaca and traveled about one hundred miles east, near the boundary of Oaxaca and Vera Cruz. During this trip, which was about two weeks in duration, he went in bathing nearly every day and while undressed was besieged with gnats and flies of which the country is full. Ten days after the first exposure to the bites of these insects he began to complain of general malaise and to have a slight rise of temperature. As soon as he began to suffer with these symptoms, he took full doses of quinine and kept the bowels moving freely with purgatives. He put himself under a physician's treatment about three weeks after the first exposure, when he began to have sharp lancinating pains in his shoulder and back. The pains were limited to four or five points where were located small discharging lesions resembling furuncles. His

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*Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10, 1909.

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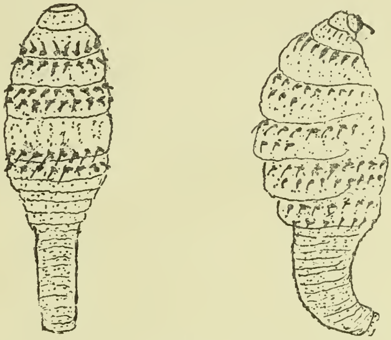
physician made a diagnosis of malaria and told him these lesions were the "malaria working out." These pains gradually increased in severity and the patient described them as being similar to pain inflicted by a punctured knife wound. The pain would only last a few seconds, but was so severe that he would jump out of bed at night, or while sitting down talking to a friend, he would have to rise suddenly from his chair. His temperature varied from 99 2-5 in the morning to 101 3-5 in the afternoon, being highest usually at 2 P. M. He was confined to his bed continuously for five days and was under "malarial treatment" and on liquid diet. He would occasionally be entirely free from fever in the morning and several times during the two or three weeks of his illness he would walk downtown and remain out of bed several hours, but would spend part of each day in bed, on account of weakness and fever. He suffered from no headache nor backache, no nose bleed nor abdominal tenderness, and no pain except that already referred to. This pain was no worse at night than in the day, and he states that rarely was there more than one lesion actively painful at a time.

I saw the patient May 12, 1908, about six weeks after the first exposure to infection. An examination of his blood for the malarial parasite was negative, as was also the physical examination of his chest and abdomen. There were present on his back and arm five lesions located as follows: one on the posterior surface of left arm at upper third, two a little internal to the left posterior axillary fold, one over the left scapula at its upper part and one in the left lumbar region. These were situated as can be readily seen where it would have been very easy for the flies to have bitten the patient.

These lesions, except the first ones mentioned, were very similar to a rather large furuncle with considerable redness and swelling, and in the center was a small round hole about the size of a pin's head through which there was a slight serosanguineous discharge. There was not the slightest pain on palpating the lesions, and patient said that when the sharp pains would come he would frequently mash them very hard without pain. The one first mentioned differed from the others in that there was practically no discharge and it had the appearance of drying up. It was hard but movable and about the size of a buckshot, feeling like a bullet under the skin. This lesion had not given him any pain for ten or twelve days before I saw him. I was unable then to diagnosticate the trouble, but decided that the places should be freely incised and drained, but as the lesion just mentioned was so circumscribed, I decided to excise the entire mass and with cocaine anesthesia I dissected out what appeared to be a small fibrous tumor that was very adherent to



Larva of dermatobia noxialis; enlarged (after Ward).

the surrounding tissue. Before incising the others, I cut open the mass and found a small larva which I decided by comparison later was undergoing a chrysalis formation. The other lesions were then incised and with slight pressure there was easily expressed a motile larva out of each lesion. The other larvæ though different in size had the following appearance: on the pear-shaped segmented bodies, which averaged in size that of a pea, there were three transverse rows of dark hairlike projections. The head, which could be thrust out or drawn in at will, was armed with two branched hooklets which evidently caused the intense pain while the larvæ were in their host. The tail was elongated and formed the stem of the pear-shaped body. This part, I was afterward told, sometimes protruded through the small opening in the skin. My patient had no unpleasant symptoms after the larvæ were removed and in a few weeks made a complete recovery.

After a consideration of this case and the literature at our command it would seem that we were dealing with a case of cutaneous myasis caused by the larvæ of the biting fly *Dermatobia noxialis.*

It appeared worth while to report the case (1) on account of the infection occurring to a citizen of the United States. (2) Because of the acute suffering and systemic effect produced by the lesions. In the literature consulted there was found no case that presented the systemic disturbance and distressing symptoms as did our patient. (3) The means of communication between the United States and other countries are continually improving and the number of people who travel in tropical and sub-tropical lands is increasing year by year, consequently the comparatively rare diseases likely to be contracted in these parts should be better known so that travelers may be warned of the dangers of exposure to biting flies and also that other patients who have contracted cutaneous myasis may be spared unnecessary suffering through failure of physicians to recognize the cause.

This report should have been accompanied by the larvæ that were removed, but unfortunately the specimens were lost. The description has been made by one who lays no claims to be a zoologist; the endeavor having been made to be practical rather than scientific.

I am indebted to Dr. J. E. Paullin for his help in enabling me to recognize the nature of the larva and to Dr. O. T. Logan for suggestions and help in looking up the literature on the subject.

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A METHOD FOR THE PREPARATION OF FLAT WORMS FOR STUDY.[a]

(Reprint from the United States Naval Medical Bulletin No. 3, Vol. 3.)

(From the laboratory of the United States Naval Medical School, Washington, D. C.)
By Passed Asst. Surg. O. J. Mink and Hospital Steward A. H. Ebeling, U. S. Navy.

We will attempt in our work to describe a simple method for the preparation and preservation of trematode and cestode material for examination by the medical practitioner.

PRESERVATION OF THE GROSS SPECIMEN.

The specimens are best obtained in a clean condition by mixing the fecal material with an amount of warm (37–40°) normal salt solution sufficient to make a thin broth. If the material is obtained at autopsy, as is usually the case with the parasites of animals used in experimental work, the intestinal contents may be washed or scraped off into the salt solution. In this warm solution the worms move about freely, and are more easily seen and transferred—especially small worms such as the Hymenolepis nana. With a pair of fine-point foreceps the worms are picked up and transferred to a second dish of warm salt solution. In this dish the worms will be found to be in a clean condition, free from mucus and fecal material. Material for sections and for the preparation of mounted segments should be taken from the salt solution and treated with the proper fixatives. The remainder of the gross material may be placed in 50–70 per cent alcohol, with or without glycerin, Zenker's solution, or a 2 per cent solution of formalin. Zenker's solution causes considerable shrinking and a rather marked yellowish discoloration. We considered the formalin mixture much better—the natural whiteness being preserved with little or no shrinkage.

PREPARATION AND SECTIONING OF MATERIAL.

Here it is of great importance to prevent curling or distortion of the worm or segment. This is best prevented by a fixative which kills rapidly, and for this we found Zenker's best. About 3 or 4 inches of the live tapeworm were taken from the salt solution and stretched out on an ordinary glass slide. By means of a pipette the

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[a] Read at the sixth annual meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10, 1909.

slide is rapidly covered with Zenker's solution. The section of the worm straightens out, hardens, and floats on the solution. It may then be transferred to a flat dish filled with Zenker's and allowed to remain here from two to twenty-four hours, according to the convenience of the worker. By cutting a little beyond the part actually desired for work, little end pieces are left which may be grasped with the forceps in subsequent manipulations. Thus the actual segments desired for study need not be touched by the forceps. The subsequent steps include the alcohol-iodine solution, graded alcohols for dehydrating, and other steps up to the melted paraffin. In blocking the specimen it seems better to place the longest and broadest surface downward and later to orient by trimming and mounting as desired. Specimens may be cut in planes (1) parallel with the long broad surface, (2) parallel with the long and perpendicular to the broad surface, (3) perpendicular to the long axis. The first and last methods give a sufficient opportunity to study all parts of the worm. There is no object in cutting sections less than 15 microns, and much time in preparation and examining will be saved if sections 25 to 30 microns are used. If too hard a paraffin is used, it will be found that the ribbons of thick sections break very easily. For 10 to 15 micron sections a 52° paraffin may be used, but for the thicker sections it is better to use a 45° paraffin. We found the most convenient stain to be a rapidly acting purely nuclear haematoxylon.

PREPARATION OF SEGMENTS FOR MOUNTING.

The specimens are washed in normal salt solution (0.85 per cent) and fixed in 2 per cent formalin for a certain time, preferably fourteen to sixteen hours. It is better not to allow the formalin to act over sixteen hours. After this the specimens are transferred to the following glucose medium, which is a slight modification of the Fabre-Domerque medium:

Sirup (glucose 48 parts, water 52 parts)	1,000 c. c. (one thousand).
Methyl alcohol	200 c. c. (two hundred).
Glycerin	100 c. c. (one hundred).
Camphor (q. s. to keep)	100 c. c. (one hundred).

The specimens may be left in this medium indefinitely, although it was found that they cleared sufficiently within four or five hours. In mounting a sufficient amount of Keisser's glycerin jelly is dropped on a slide and the specimen transferred to this, care being taken not to introduce air bubbles. A flamed cover glass finishes the mount. After the glycerin jelly hardens a few coats of gold size applied consecutively around the cover glass furnishes rigidity and improves the general appearance of the preparation. Concave slides are more desirable when the specimen is of uneven thickness or rather thick throughout.

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The American Society of Tropical Medicine.

1910.

HENRY B. WARD
CASE UNIVERSITY

The American Society of Tropical Medicine.

Papers Read Before the Society and Published under Its Auspices.

Volume 5, 1910.

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Articles of Association.

CHARTER.

Be it known that the subscribers, having associated themselves together for the purpose hereinafter mentioned, and being desirous of becoming incorporated agreeably to existing laws of the Commonwealth of Pennsylvania providing for the incorporation and regulation of certain corporations, approved April 29, 1874, and its supplements, do hereby declare and certify that the following are the purposes, objects, articles, and conditions of their said association, for and on which they desire to be incorporated.

I. The name of the corporation shall be: AMERICAN SOCIETY OF TROPICAL MEDICINE.

II. The purpose for which the corporation is formed is to advance the knowledge of tropical diseases by encouraging original research by its members and others; collecting and recording facts ascertained by such researches, and disseminating information thereof by discussion among its members and by the publication of papers read before the society.

III. The corporation is to exist perpetually.

IV. The location of the Secretary's office shall be in the city of Philadelphia.

V. The names and residences of the subscribers hereto are as follows: Thomas H. Fenton, M.D., 1319 Spruce St., Philadelphia; Judson Daland, M.D., 317 South 18th St., Philadelphia; Joseph McFarland, M.D., Medico-Chirurgical College, Philadelphia.

V. The corporation is to be managed by a Council of five members and a President and Secretary who shall be ex-officio members of the Council. In addition thereto there shall be annually chosen a Treasurer, two Vice-Presidents, and an Assistant Secretary. The names and residences of those chosen for the first year are: Thomas H. Fenton, M.D., Philadelphia, President; James C. Wilson, M.D., and James M. Anders, M.D., both of Philadelphia, Vice-Presidents; E. B. Gleason, M.D., Philadelphia, Treasurer; Joeph McFarland, M.D., Philadelphia, Secretary; John M. Swan, M.D., Philadelphia, Assistant Secretary; and John V. Shoemaker, M.D., Hobart A. Hare, M.D., Roland G. Curtin, M.D., Judson Daland, M.D., Orville Horwitz, M.D., all of Philadelphia, Councillors.

VII. The Corporation has no capital stock.

American Society of Tropical Medicine.

BY-LAWS.

Recommended by Council at its meeting, March 20, 1903, and adopted May 25, 1903.

ARTICLE I.—The members of the Society shall be of three classes: *Active, Corresponding,* and *Honorary.*

Any regular American physician or scientist interested in the study of tropical diseases shall be eligible for *Active membership.*

Any regular physician or scientist not a resident of the United States, who has contributed to the knowledge of tropical diseases, shall be eligible for *Corresponding membership.*

Any scientist who has made eminent contributions to tropical medicine shall be eligible for *Honorary membership.*

The number of active members shall be limited to 200. Candidates for membership shall be elected until 1904 by the Council, and thereafter by ballot at the annual meeting upon recommendation by the Council.

ARTICLE II.—The dues shall be fixed each year by the Council, but shall not be increased beyond $5.00 without approval by the Society at its annual meeting.

The regular dues shall be paid by active members only.

The corresponding and honorary members shall be exempt from dues.

ARTICLE III.—The officers shall consist of a President, two Vice-Presidents, a Treasurer, a Secretary, an Assistant Secretary, and a Council of five members. They shall perform the customary duties of such officers.

The Council shall have general supervision of the affairs of the Society, and shall meet from time to time as they determine. The

President and the Secretary shall be ex-officio members of the Council. In 1905 three Councillors shall be elected for two years and two Councillors for one year. Thereafter each Councillor shall be elected for two years. In case of death or resignation of any officer or Councillor of the Society, the Council shall be empowered to fill such vacancy until the next annual meeting.

ARTICLE IV.—There shall be an annual meeting and such other scientific or business meetings as the Council shall determine.

The annual meeting shall be known as the business meeting when the election of officers for the ensuing year shall be held, and routine and other business transacted.

ARTICLE V.—These By-Laws may be amended by a two-thirds vote of the Society at its annual meeting as suggested by Council, provided each amendment has been offered to the Council one month previously, and recommended by it. Due notice of such contemplated changes to be sent out with the announcement of the annual meeting.

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1907. Dr. J. Percival Mackie, Uganda.
1904. Dr. Jesus E. Monjaras, Mexico City.
1904. Dr. W. E. Park, Soo Chow, China.
1907. Sir Allan Perry, Colombo, Ceylon.
1907. Major Leonard Rogers, Calcutta.
1907. Dr. A. T. Stanton, Kuala Lumpur, Federated Malay States.
1906. Dr. John M. Swan, Canton, China.

Is Hemoglobinuric Fever a Manifestation of Malaria or a Disease *Sui Generis?*

CHARLES F. CRAIG, M.D.
WASHINGTON, D. C.

IS HEMOGLOBINURIC FEVER A MANIFESTATION OF MALARIA OR A DISEASE *SUI GENERIS*?*

CHARLES F. CRAIG, M.D.
WASHINGTON, D. C.

The present condition of uncertainty regarding the etiology of hemoglobinuric fever may well be likened to that regarding the etiology of kala-azar ten years ago, and the history in this respect of the latter disease is of peculiar interest to the students of hemoglobinuric fever, because it furnishes an excellent example of how preconceived opinions influence the work of careful observers, and illustrates the fallibility of deductions regarding the etiology of any disease when influenced by such opinions.

For many years kala-azar was regarded as a persistent form of malarial infection, or a form of malarial cachexia. As late as 1896 Leonard Rogers considered it to be a fatal form of malaria, while Ronald Ross, in 1898, stated it as his belief that it was a form of malarial fever complicated by some secondary infection. Giles, after careful study, had come to the conclusion that kala-azar was due to *Ankylostoma duodenale,* and Bentley, in 1903, regarded it as a severe form of Malta fever. The discovery of the parasite now known as *Leishmania donovani* by Leishman, which was at once confirmed by Donovan, decided the etiology of kala-azar, and proved how erroneous were the theories regarding its malarial origin.

For years the study of hemoglobinuric fever has been greatly influenced by the theory that it is due to malarial infection, and much of the data which has accumulated concerning this disease has been published by believers in the malarial theory, or in the theory that it is due to quinin. While the literature contains many authentic instances which absolutely disprove both of these theories their adherents appear to have overlooked or undervalued them, and to-day the general opinion of the medical profession appears to be in favor of the theory that hemoglobinuric fever is due to malarial infection.

To one who carefully studies the literature of this disease it is evident that, in reality, its etiology is unknown; that the preconceived opinions regarding its malarial nature and its relation to quinin have greatly hindered investigation, and influenced those who have endeavored to study its etiology from an experimental standpoint; and that there is every reason to believe that further research will result in proving that hemoglobinuric fever is a specific disease. The further we inquire into its etiology, pathology, and symptomatology, the more must we become convinced that the malarial nature of the condition is far from demonstrated, and that the evidence points to its being a specific disease caused by an undiscovered parasite.

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Before considering in detail the theories regarding the etiology of this disease, I desire to call attention to the fact that not a few of the cases reported in the literature as hemoglobinuric fever are in reality other forms of hemoglobinuria or hematuria, having no relation to the true disease. Therefore, in the study of this condition it is most important to be sure that we are dealing with true hemoglobinuric fever rather than other conditions which sometimes very closely simulate it. Thus we must differentiate paroxysmal hemoglobinuria, hematuria, the hemoglobinuria following the administration of poisonous drugs, and the rare instances of idiosyncrasy to quinin, resulting in the production of this symptom. True hemoglobinuric fever has a definite symptomatology and is readily recognized by those living in the endemic areas, and all cases which do not agree with the clinical characteristics which have been described by many careful observers in blackwater fever regions should be regarded with suspicion. The mere fact that a patient passes a little bloody urine is very insufficient proof that he is suffering from hemoglobinuric fever, and yet the literature contains numerous reports in which this was the only symptom present, and such cases have been used to support the several theories regarding the etiology of the disease. In this contribution I have been careful to cite only those reports in which the patients described were without doubt suffering from hemoglobinuric fever.

There are three principal theories regarding the etiology of this disease; first, that it is due directly or indirectly to malarial infection; second, that it is due to quinin; and third, that it is a specific disease. Each has its enthusiastic supporters, but, as a matter of fact, not one of them rests on a firm foundation as regards absolute proof.

1. THE MALARIAL THEORY

PRESENT STATUS OF THEORY

The theory that hemoglobinuric fever is due directly or indirectly to malarial infection is very old, and is supported by many of the greatest authorities on the fevers of tropical and subtropical countries. The names of Plehm, Stephens, Bentley, Christophers, Zieman, Mannaberg, and others of equal reputation, are associated with this theory, and the following quotations from Stephens well illustrate its present position. Stephens says:[1]

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[1] Stephens, J. W. W.: Blackwater Fever, in Allbutt and Rolleston's A System of Medicine, London, 1907, ii, part 2, p. 295.

> The etiology of blackwater fever may be summed up by saying that it is malarial in nature, *i. e.*, that it can only occur in those who are either suffering from, or have quite recently become infected with, malaria, and that the onset of the disease is induced most commonly, though not invariably, by quinin.

Again, in another contribution, he says:[2]

> We may sum up the etiology of blackwater fever somewhat in this way: It is not a disease *per se*, but rather a condition of blood in which quinin, other drugs, cold, or even exertion, may produce a sudden destruction of red cells. The condition is produced only by malaria, and generally by repeated small attacks, insufficiently treated by quinin. In such cases of chronic malaria (*i. e.*, in those suffering from anemia with repeated attacks of fever and repeated doses of quinin) blackwater fever sooner or later almost certainly supervenes, at least in tropical climates. The two main factors in hemoglobinuria are, then, malaria and quinin.

Because of the objections to the malarial theory which have arisen from time to time, its adherents have modified their views, until we now have the rather amusing spectacle of a theory supported by numerous authorities, each of whom, however, explains the relation of the two diseases in a different maner. That this is true is evidenced by the following modifications of the theory which are supported by different investigators: Hemoglobinuric fever is caused by estivo-autumnal plasmodia; it is caused by a special species of malarial plasmodium; it is a peculiar form of pernicious malaria, which may be produced by any one of the species of plasmodia; it is due to malignant tertian infection accompanied by congestion of the liver; it is due to a toxin produced by the malarial plasmodia; it is due to a toxin resulting from the destruction of the red corpuscles by the plasmodia; it is due to changes in the blood caused by previous malarial infection; it is due to a condition of susceptibility to quinin brought about by malarial infection; it is due to an autolysin produced in the blood by malarial infection; it is an idiosyncrasy of certain malarial patients; and, finally, it is simply a complication of malarial fever.

The points which are usually urged in support of the malarial theory of the origin of hemoglobinuric fever are the following:

1. The occurrence of the disease only in malarial regions.
2. The presence of plasmodia in the blood, during the period immediately preceding, or during the first days of an attack.
3. The fact that most patients who develop hemoglobinuric fever have suffered previously from malaria.
4. The more frequent occurrence of the disease in localities where pernicious forms of malaria occur.
5. The fact that long residence in a malarial locality is required before the disease can develop.
6. The fact that there is an increase in the large mononuclear leukocytes similar to that occurring in malarial infection.

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[2] Stephens, J. W. W.: Blackwater Fever, in Osler's Modern Medicine, Philadelphia, 1907, i, 455.

In order to understand clearly the relation of malaria to hemoglobinuric fever, it is necessary to consider each of the points mentioned; and I believe that a careful survey of the evidence will carry the conviction that not one of them can be accepted as proving that the disease is of malarial origin, and that taken together they speak as strongly in support of the specific theory as they do of the theory under discussion.

THE GEOGRAPHICAL DISTRIBUTION OF HEMOGLOBINURIC FEVER AND MALARIA

It is an accepted fact that hemoglobinuric fever occurs only in regions where malarial infections are endemic, but does this prove that the disease is of malarial origin? While the disease occurs only where malarial infections are endemic, there are many regions intensely infected with malaria where this disease is unknown. This fact must be admitted by every student of the disease, and is most difficult of explanation, if we accept the malarial theory. Hemoglobinuric fever is very prevalent and wide-spread in Africa, common in Sicily and Sardinia, but rare in Italy. In India the disease occurs in very limited localities, and similar regions in that country, as regards climatic and other known conditions, and as intensely infected with malaria, are free from hemoglobinuric fever. In Italy, even in the regions where the malarial fevers are most pernicious, this disease is either absent, or occurs very rarely. In fact, it may be said that Africa is the only country in which hemoglobinuric fever is generally distributed, for, in all the other countries in which it occurs, its distribution is strictly localized, while there are many countries in which pernicious forms of malaria occur, but in which blackwater fever is unknown, or occurs only in the form of imported cases. In a personal letter Dr. Prado, health officer of Trinidad, informs me that while malaria is both prevalent and severe in Trinidad and the island of Tobago, blackwater fever is common in Tobago and very rare in Trinidad, occurring only on a part of the coast-line adjacent to Tobago. and frequented by laborers from that island.

Even in the countries in which this fever occurs, there are many regions as intensely infected with malaria which are free from the disease, although only a comparatively short distance from the endemic foci. Such regions occur in our own country, in some of the southern states, and in Italy hemoglobinuric fever is limited to very restricted localities, while some of the worst malarial portions of that country have never presented a single instance of this disease. The same is true of India, of the Straits Settlements, the islands of Polynesia, the West Indies, and the countries of South America.

The almost complete absence of hemoglobinuric fever in the Philippine Islands is an excellent illustration of the fact that a most malarial country may be free from the disease. In the Philippine Census[3] for 1902, the total number of deaths from malarial fever is stated to have been 118,476, or 26.8 per cent. of all deaths, the death-rate being seventeen per thousand, and yet not a single death is recorded as being due to hemoglobinuric fever. How is it possible to explain this fact in accordance with the theory that the disease is caused by malarial infection?

Christophers and Bentley[4] believe that hemoglobinuric fever occurs only in countries where the malarial infections are intense, and that such infections, no matter what species of plasmodium causes them, may give rise to the disease. I believe that all will admit that the vast majority of intense or malignant malarial infections are caused by the estivo-autumnal plasmodia, but even in regions where the most severe estivo-autumnal infections are prevalent, hemoglobinuric fever is often absent. At Camp Stotsenburg, in the Philippines, one of the most intensely malarial regions of which we have record, where, within six months, there were more than thirty deaths from pernicious malaria among the natives in the vicinity, a case of hemoglobinuric fever has never been known to occur, and the natives informed me that they had never heard of a single instance of the passage of bloody urine during an attack of fever. If intense malarial infection is necessary for the production of hemoglobinuric fever, then in this locality one would expect to meet instances of the disease, but it is unknown. This is equally true of every other intensely malarious region in the Philippine Islands and of similar regions in many other parts of the world. Tables 1, 2 and 3 illustrate the intensity of malarial infection in some of the islands, provinces and towns of the Philippines, and prove that intensity of malarial infection has nothing to do with the production of hemoglobinuric fever.

It is evident from these tables that the Philippines are intensely infected with malaria and that the death-rate is high from that disease; but hemoglobinuric fever is practically unknown. I know from personal observation that the death-rate as given for some of these towns is not excessive, and that there are many towns in the Philippines in which malaria causes more than 50 per cent. of the death-rate.

Christophers and Bentley state that certain conditions may be present in blackwater regions which are not present in other malarial regions, but so far as climatic conditions are concerned this is not so, for in almost every country in which hemoglobinuric fever occurs the climatic conditions are the same in the blackwater regions as in others. So far as other conditions are concerned, it is enough to say that we are absolutely ignorant of what they are, and therefore they cannot be used in proving the malarial hypothesis. The fact remains that intense estivo-

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[3] Census of the Philippine Islands, Washington, 1905, iii, 70.

[4] Christophers, S. R., and Bentley, C. A.: Blackwater Fever, Scient. Mem., Med. and San. Depts. Govt. India, Simla, 1908, N. S., No. 35.

TABLE 1.—TOTAL DEATHS AND DEATHS FROM MALARIA IN CERTAIN ISLANDS OF THE PHILIPPINES

Island.	Total Deaths.	Deaths from Malaria.
Luzon	248,831	60,516
Cebu	18,955	6,356
Panay	75,535	22,478
Mindanao	12,572	6,423
Marinduque	3,222	1,466
Guimaras	1,302	479
Baliran	1,247	423

TABLE 2.—POPULATION, TOTAL DEATHS AND DEATHS FROM MALARIA IN THE PROVINCES OF THE PHILIPPINE ISLANDS

Province.	Population.	Total Deaths.	Deaths from Malaria.	Pr. Ct. of All Deaths.
Albay	240,326	11,564	3,103	26.8
Antigue	134,166	7,411	3,181	42.9
Batangas	257,715	34,257	13,216	38.5
Capiz	230,721	15,564	3,254	20.9
Cebu	653,727	20,920	7,020	33.6
Iloilo	410,315	51,153	16,572	32.4
La Laguna	148,606	15,918	4,877	30.6
Misamis	175,683	9,038	4,961	54.9
Pampanga	223,754	14,383	3,247	22.6
Pangasinan	397,902	24,701	6,531	26.4
Samar	266,237	13,614	3,913	28.7
Tayabas	153,065	9,418	3,501	37.2
Davao	65,496	557	256	46.
Marinduque	51,674	3,222	1,466	45.
Masbate	43,675	1,881	811	43.1
Nueva Vizcaya	62,541	1,228	511	41.6
Dapitan	23,577	397	152	38.3
Romblon	52,848	1,422	531	37.3
Surigao	115,112	3,304	1,200	36.3
Negros Oriental	201,494	5,972	2,135	35.8
Tarlao	135,107	7,088	2,453	34.6

TABLE 3.—POPULATION, TOTAL DEATHS AND DEATHS FROM MALARIA IN PHILIPPINE TOWNS *

Town.	Population.	Total Deaths.	Deaths from Malaria.
Angeles	10,646	431	119
Apalit	12,206	771	208
Anao-aon	1,481	90	59
Bacuag	2,938	100	77
Camiling	25,243	1,288	513
Concepcion	12,593	600	211
Gerona	13,615	635	257
Floridablanca	7,001	623	328
Jiminez	7,187	1,066	1,019
Misamis	5,525	310	290
Mabalacat	7,009	201	126
Mainit	1,588	123	84
Orequita	15,156	1,650	1,572
Palapag	9,609	200	122
Pasig	4,830	296	110
Pambujan	6,439	331	174
Porac	8,487	490	251
San Carlos	27.166	1,856	744
Tago	3.298	129	60
Taranguan	6,184	549	234
Tigao	946	16	8
Urdaneta	20,544	1,378	498

* All of these tables are compiled from the Philippine Census.

autumnal infections are prevalent in nearly all tropical regions, while hemoglobinuric fever is restricted to certain countries, and in these countries, as a general rule, it occurs only in limited localities.

In regions in which hemoglobinuric fever occurs, the disease may be limited to certain very small areas, even to certain houses, and so-called "blackwater fever houses" have been reported by Daniels, Christophers and Bentley, and others. Christophers and Bentley report instances in which two or more cases of the disease have occurred in the same house, while other houses in the vicinity remained free from the infection. Because these houses were located in malarial localities, these authors believe that the disease must have been of malarial origin, but it would appear more reasonable to believe that some specific cause was present in these houses, or that the transmitting agent, perhaps a comparatively rare insect, was to be found only in the houses mentioned.

Another fact that speaks against the theory that hemoglobinuric fever is of malarial origin is that, in some of the countries where it is now prevalent, it has only recently been observed, although malarial fevers have been present for centuries. This fact must be admitted by every one who is conversant with the literature of the disease. A. Plehn[5] states that it is only recently that the disease has appeared on the west coast of Africa, where it is increasing in frequency yearly; and the same is true of India, where it is now prevalent in limited localities. The very extensive and valuable works of such men as Carter and Fayrer contain no mention of the occurrence of this disease in India in their time, and it is impossible to believe that these keen clinical observers could have overlooked a disease so striking in its symptomatology as is hemoglobinuric fever. If, then, this fever be due to malaria, how is it possible to explain its recent appearance in countries where for centuries the most intense malarial infections have existed? While it must be admitted that the disease occurs only in malarial localities, it can by no means be admitted that, therefore, the disease is of malarial nature. Many other acute infectious diseases are most commonly observed in regions infected with malaria, such as amebic dysentery, beriberi, infections with the various intestinal parasites, yellow fever, kala-azar, sleeping-sickness, and most tropical diseases, and some of them are practically limited to malarial localities, especially kala-azar, sleeping-sickness, and yellow fever; but we do not for this reason conclude that they are caused by malarial infection. The absence of hemoglobinuric fever from many intensely malarial regions and its presence in very limited localities in the regions in which it does occur, together with its recent appearance in certain countries, is very strong presumptive evidence that it is not due to malaria, and I believe that the unprejudiced observer must admit that the geographical distribution of this disease, far from proving its malarial origin, points directly to its specific nature.

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[5] Plehn, A.: The Cause, Prevention and Treatment of Hemoglobinuric Fever in Warm Countries, Jour. Trop. Med. and Hyg., 1908, ii, 294.

LENGTH OF RESIDENCE AND HEMOGLOBINURIC FEVER

It is a well-known fact that most victims of hemoglobinuric fever have resided for some time in the infected locality, and this fact is used as an argument in favor of the malarial theory, it being claimed that repeated malarial attacks are necessary for the production of this disease, and that therefore long residence in a malarial locality is essential. While it must be admitted that most cases of hemoglobinuric fever occur after the first twelve months of residence in the infected district is completed, many instances have been reported in which the symptoms appeared within less than three months after entering the infected territory, and in individuals who had never suffered from malarial infection, so far as could be ascertained; while a few cases have been reported in which the disease appeared within a few days after entering the blackwater district. I shall mention only a few of the authors who have reported instances of this kind, but the literature contains a great many such cases. Poole[6] found that, of fifty-six cases studied by him, no less than seventeen occurred in individuals who had been in the infected district less than one year. Reynolds[7] describes one instance in which the patient developed the disease within ten weeks after reaching the infected region, and others in which the disease appeared in four months, seven months, and nine months. Berenger-Feraud[8] observed one case in which the disease developed within three months, and ten in which it developed within one year; while Christophers and Bentley[4] observed one case developing within six months, and eight within one year after exposure in infected districts. Manson[9] states that instances of infection have been observed during the second and third months after arrival in infected regions, and in the last edition of his work on tropical diseases, he says (p. 235):

> There are many cases on record in which blackwater fever occurred before any kind of "malaria" had manifested itself. Plehn, Scott, Ritchie, Cardamatis, Lynch, Hearsey, Daniels and others have reported cases of blackwater fever in robust, healthy individuals, who were attacked within two or three months of their arrival in a blackwater fever country. I have frequently been told by officers in the African colonial service that the attack of blackwater fever for which they were invalided suddenly developed while they appeared to be in perfect health and without any malarial antecedents.

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[6] Poole, W.: An Analysis of Fifty-six Cases of Blackwater Fever, Jour. Trop. Med., 1899, i, 145.

[7] Reynolds, G. F.: Blackwater Fever, Some Cases and Notes, Jour. Trop. Med., 1899, i, 16.

[8] Berenger-Feraud: De la fièvre bileuse mélanurique des pays chauds, Paris, 1874, Ed. I.

[9] Manson, Sir Patrick: Tropical Diseases, New York, 1907, Ed. 4.

F. Plehn[10] saw two patients suffering from hemoglobinuric fever which developed within four or five weeks after their arrival in Cameroon, neither of whom had suffered from malarial infection. Gross saw a patient who developed the disease within fifteen days after reaching Gaboon, and who had never had malaria. Brem[11] saw one patient who developed the disease after only two months' residence on the Isthmus of Panama; and Ziemann[12] one case occurring twenty-seven days after reaching the infected locality, and another within six weeks. Dr. Prado, in a personal communication, informs me that blackwater fever attacks new arrivals in Tobago.

It should be remembered that these patients had not resided previously in infected districts and that in most of them no history of a previous malarial infection could be obtained. It is thus evident that a long residence in the infected district is not necessary for the development of hemoglobinuric fever and that the statement of Christophers and Bentley that many months or years of exposure to the infection is required before blackwater fever can occur is unwarranted in the light of the evidence which has accumulated regarding this question.

While it is true that the disease may occur in individuals who have been exposed only a short time, it is also true that the vast majority of cases of this disease occur between the first and third years of residence, thus proving that length of residence favors the development of the disease. As the regions in which hemoglobinuric fever occur are also malarial, it follows that most of the victims of this disease have also suffered from malarial infection, but this does not prove that malaria is the etiological factor, as will be shown in the following section.

PREVIOUS MALARIAL INFECTION AND HEMOGLOBINURIC FEVER

A history of previous malarial infection may be obtained in a large majority of cases of hemoglobinuric fever, but not in all. Many instances have been reported of the occurrence of this disease in individuals who had never suffered from malaria, and in whom no plasmodia could be found at the onset of the disease. The fact that the disease occurs most frequently in malarial localities makes it inevitable that most patients suffering from it have previously suffered from malaria, or, indeed, may be suffering from both diseases at the same time, for, from what we know of this disease, it is very rare as compared with malaria, and therefore most patients residing long enough in a locality to develop the disease have already become infected with malaria. It has been asserted by the most ardent advocates of the malarial theory that not a single case is on record of the occurrence of hemoglobinuric fever in a patient who had not previously had malaria, but such an assertion can be made only by one who is but very little acquainted with the literature, for numerous cases are recorded in which the disease developed in healthy individuals within two or three months after reaching infected districts and in whom there had never been any symptoms of malarial fever. That in most of these cases the disease could not have been present in a latent form is proved by the fact that many of the patients came from countries where malaria was not present, especially from England, and had not been exposed during the sea journey. Such cases have been reported by Manson,[9] Sambon,[13] Cardamatis,[14] Curry,[15] Ritchie,[16] Murri,[17] Stalkarrt,[18] Daniels,[19] and many others. The theory of Stephens and Christophers[20] that the disease is due to an unstable condition of the blood brought about by repeated malarial infection is thus disproved. It is a well-known fact that many patients suffering from hemoglobinuric fever do not present the appearance and symptoms of malarial cachexia, although, if this theory were true, it would be expected that most malarial cachectics would develop hemoglobinuric fever. It is also a well-known fact that this disease may develop during the first outbreak of malaria, and Deaderick[21] states that while hemoglobinuric fever generally occurs only after repeated malarial attacks, it may develop during the first attack. It is more than probable that such instances are in reality combined malarial and hemoglobinuric fevers.

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[10] Quoted by A. Plehn, Jour. Trop. Med. and Hyg., 1908, ii, 294.

[11] Brem. W. V.: Malarial Hemoglobinuria, Jour. Am. Med. Assn., 1906, xlvii, 1992.

[12] Zieman, H.: Malaria, Mense's Handbuch der Tropenkrankheiten, Leipsic, 1906, iii (Halband I), 270.

Again, if repeated malarial attacks result in an unstable condition of the blood which causes hemoglobinuria, it is justifiable to ask why it is that such an unstable condition occurs as the result of malaria, only in restricted localities. In some of the most intensely malarial regions known a person may suffer for years from repeated attacks of malaria, and yet never develop hemoglobinuric fever, the disease being unknown in these regions. I have already called attention to the fact that climatic and all other known conditions are the same in these regions as in the

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13. Sambon, L. W.: The Etiology and Treatment of Blackwater Fever, Jour. Trop. Med., 1899, i, 243, 262, 295.

14. Cardamatis: La fièvre bilieuse hémoglobinurique, Paris, 1902, Ed. 1.

15. Curry, Joseph J.: Blackwater (Hemoglobinuric) Fever, Jour. Am. Med. Assn., 1902, xxxviii, 1130.

16. Ritchie: Cited by Manson, Tropical Diseases, p. 235.

17. Murri: Cited by Deaderick, A Practical Study of Malaria.

18. Stalkarrt, W. H. S.: Hemoglobinuric Fever and Paludism, Brit. Med. Jour., 1899, ii, 654.

19. Daniels, C. W.: Rep. Malarial Com. Roy. Soc., London, 1901, Series 5, p. 46.

20. Stephens, J. W. W., and Christophers, S. R.: Rep. Malarial Com. Roy. Soc., London, 1901, Series 5, p. 17.

21. Deaderick, W. H.: A. Practical Study of Malaria, Philadelphia, 1910, Ed. 1.

endemic centers of hemoglobinuric fever, so that it is very difficult to explain this discrepancy on the malarial hypothesis. The advocates of this theory, however, have urged that unknown conditions may be present, but this is simply begging the question, and admitting that malaria differs in this respect from any other known disease. So far as I am aware, there is no acute infectious disease which gives rise to a striking symptom-complex in some regions, while in others this symptom-complex never occurs, although in the latter regions the disease is as intense and pernicious in character. Yet we are asked by the adherents of the malarial theory of the origin of hemoglobinuric fever to believe that malarial infection produces blackwater fever in certain districts, while in similar districts this symptom-complex never occurs, although the malarial infections are of the same type.

To one who has studied the literature, however, it is perfectly evident that repeated malarial infection is not necessary for the production of hemoglobinuric fever, as many instances of the disease have occurred in which past malarial infection could be definitely proven not to have existed. The reports of Murri, Mould, F. Plehn, and Gros, as well as others, prove that the disease may occur in persons who have never suffered from malaria, while those of F. Plehn, Goltman and Krause, and Brem, prove that it may occur during the first symptoms of a malarial infection. It is therefore justifiable to conclude that hemoglobinuric fever is not due to repeated attacks of malarial fever, and that in many instances no previous malarial infection has existed.

THE OCCURRENCE OF MALARIAL PLASMODIA IN HEMOGLOBINURIC FEVER

The presence of malarial plasmodia in the blood of a large proportion of patients suffering from hemoglobinuric fever is considered by many authorities as proving its malarial origin; but many other conditions are frequently encountered in malarial regions in which the plasmodia may be found in the blood, but which are never considered as being due to malarial infection. The fashion of considering an organism as causative merely because it is frequently associated with a disease has generally resulted in disaster, and in the case of kala-azar, Malta fever, and sleeping-sickness, greatly delayed the discovery of the real cause.

It is but natural that, in a malarial region, patients suffering from this disease should present malarial plasmodia in their blood in many instances. The mere presence of such plasmodia, or of pigment in the tissues, does not prove that the condition is due to malarial infection, and the absence of both pigment and plasmodia in well-authenticated cases of hemoglobinuric fever proves conclusively that malaria cannot be considered as the direct cause of the disease.

As regards the frequency of the occurrence of plasmodia in the peripheral blood in hemoglobinuric fever, it may be said that it varies in different localities and with the time that the blood is examined. I have collected 273 cases in the literature, of which 109, or 40 per cent., showed malarial plasmodia in the blood. The researches of Stephens and Christophers[4, 20] and of Mannaberg[22] have shown that the number of patients presenting plasmodia in their blood varies with the time of examination, 95 per cent. of patients showing them the day before the attack; 60 to 70 per cent. showing them the day of the attack; and only 17 to 20 per cent. showing them the day after the attack. This fact has been used in contradicting the proofs of the absence of the plasmodia in cases of hemoglobinuric fever, but there are many cases on record in which the blood was examined before, during, and after the attack, and no plasmodia could be found, even puncture of the spleen being attended with a negative result. While 95 per cent. of hemoglobinuric fever patients may show plasmodia in their blood in some regions the day before an attack, it is equally true that in other blackwater regions 100 per cent. have not shown them, for it must be remembered that it is but seldom that the blood happens to be examined at this time, and that, therefore, the number of observations are very small.

From the reports of many investigators it is justifiable to state that cases of hemoglobinuric fever have occurred in which malarial plasmodia were not present, so far as could be determined, either before, during, or after the attack, while in fatal cases no evidence of malarial infection was found at autopsy. Many of these cases are reported by staunch advocates of the malarial theory and the evidence, therefore, is not affected by an unconscious personal equation.

Poole[6] found that some of his cases were negative for plasmodia either before, during, or after an attack of blackwater, although the examination was made most carefully; Barratt and Yorke[23] carefully examined twenty cases of hemoglobinuric fever, and found that nineteen of them were negative for plasmodia on the first day of the disease. They say:

> On one occasion it happened that an examination of the blood was made within two hours of the establishment of hemoglobinuria and one hour before the administration of quinin. In this case no parasites could be recognized after careful search. It can be asserted, therefore, that in this case, hemoglobinuria was not dependent on the hemolysis, in the peripheral blood, of the red cells containing the parasites.

As regards the presence of pigment or parasites in the organs of fatal cases, Barratt and Yorke say:

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22. Mannaberg, J.: Die Malaria-Krankheiten, Nothnagel's Encyclopedia, Berlin, 1899.

23. Barratt, J. O. W., and Yorke, W.: An Investigation Into the Mechanism of the Production of Blackwater Fever, Ann. Trop. Med. and Hyg., 1909, Series T. M., iii, 152.

> The presence of malarial pigment in the blood-vessels of the organs, usually the kidneys, has been described by several authors. In the three cases in which we had an opportunity of studying this point, no pigment was found in the kidneys, spleen, or liver, nor could malarial parasites be recognized in the blood-vessels of these organs.

In one of their cases the patient had never suffered from malaria to his knowledge. In sixteen of the twenty cases the onset of hemoglobinuria was preceded for several days by more or less general disturbance. Regarding this they say:

> This lasted in fourteen attacks from one to seven days, and in two attacks ten and twenty-one days, respectively. The preliminary illness was regarded as malarial, but in only one case were malarial parasites found before the onset of hemoglobinuria.

This statement effectively disposes of the assertion that malarial plasmodia are always present in the peripheral blood before the onset of blackwater fever. Barratt and Yorke performed splenic puncture in six of their cases and in none of them were they able to find parasites or pigment in the material obtained; while they examined four of their patients on the first day of hemoglobinuria, giving the peripheral blood the most careful scrutiny, and did not find plasmodia in one of them.

Koch[24] described twenty-three cases of hemoglobinuric fever in which no plasmodia could be found, although some of them were fatal infections, while in four cases he found the plasmodia both before and after the attack, thus proving that their absence is not entirely due to blood destruction, as claimed by Christophers and Bentley. Koch says:

> We thus perceive that the malarial plasmodia do not perish in blackwater fever attacks; that during the attack they are either entirely absent or show no remarkable increase; that, even if they are present in great numbers, no hemoglobinuria need develop. Therefore, how can one still assert that blackwater fever is caused by malarial parasites?

Mould[25] reports a case of hemoglobinuric fever which developed in a hospital; the patient, in whose blood no plasmodia could be found, never having suffered from malarial infection. Curry[15] reports two cases in which neither during the attack nor at autopsy could any evidence of present or past malarial infection be obtained, the tissues being free from pigment and parasites, and the blood likewise. In both cases the blood was examined during the first day of the attack. He describes another case in which no parasites were found, although the blood had been carefully examined for ten days preceding the attack.

Daniels[19] was unable to find plasmodia in a single one of sixteen cases which he investigated, either during or after the period of hemoglobinuria; Christophers and Bentley,[20] while agreeing that the manifestations of hemoglobinuric fever should occur only during coincident malarial infection, in their own report describe cases in which even the splenic blood did not contain parasites. Case 20 showed no parasites, though examined during the first day of the attack, and Case 26 was also negative, while the splenic blood of other patients showed a very few plasmodia. Their results dispose of the theory that the plasmodia are really very numerous in this disease, but are not discovered because they are localized in the internal organs, especially the spleen.

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[24] 24. Koch, R.: Blackwater Fever (Hemoglobinuria), Jour. Trop. Med., 1899, i, 333.

[25] 25. Mould, Captain: Cited by Sambon, Jour. Trop. Med., 1899, i, 243, 262, 295.

Newell,[26] though an ardent advocate of the malarial theory, did not find plasmodia in any of the five cases described in his book, so far as he states. Van der Scheer,[27] Hanley,[28] Thin,[29] Howard,[30] Oeconomou,[31] Le Dantec,[32] and Gaudacheau,[33] all report cases in which plasmodia were not found in the blood during an attack of hemoglobinuric fever, and many of them were negative before the onset of hemoglobinuria.

Whipple[34] has recently contributed a valuable study of the pathology of hemoglobinuric fever, and believes that malaria always precedes this disease and predisposes to it, but the evidences of malarial infection in most of his cases are slight and would appear to be insufficient to prove the importance of previous malarial infection. He studied nine cases of hemoglobinuric fever at autopsy, in only two of which were plasmodia demonstrated, and compares the pathological findings with three cases of combined hemoglobinuric fever and pernicious malaria, and with five cases of pernicious malaria. He believes that the pathological findings in the hemoglobinuric fever cases "show a great similarity to those of the pernicious malaria cases and indicate that a malarial infection is an unfailing factor in all cases." In seven of the nine cases of uncomplicated hemoglobinuric fever the only evidence of malaria consisted in a small amount of pigment in the leukocytes of the spleen, kidney, and liver, and this pigment was present in such small amount in two cases that Whipple says (p. 226):

> In autopsy 1,168 and 1,169 malarial pigment is in very small amounts and is only found in the various organs after a long search. It is included in phagocytes. The second case shows a few coarse grains of malarial pigment in the cortex of the portal gland, indicating a previous malarial infection. We cannot imagine any ferment capable of rapidly dissolving the melanin which is set free by the sporulation or death of the malarial parasite. So it seems conclusive

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26. Newell, C.: Blackwater Fever (Bilious Malignant Tertian Ague), London, 1909, Ed. 1.

27. Van der Scheer: Cited by Mense: Arch. f. Schiffs- u. Tropen-Hyg., 1899, iii, 80.

28. Hanley: Jour Trop. Med., 1899, i, 85.

29. Thin: Brit. Med. Jour., 1900, ii.

30. Howard: Jour. Trop. Med., 1907, x, 81.

31. Oeconomou: Cited by Cardamatis, Progrès Méd., 1902, xx, 201.

32. Le Dantec: Pathologie exotique, Paris, 1905, Ed. 1.

33. Gaudacheau: Cited by Deaderick, A Practical Study of Malaria.

34. Whipple, G. H.: Blackwater Fever and Pernicious Malaria in Panama, Malaria, 1909, i, 215.

that there could have been but very few malarial parasites in the vascular system of these two patients. This would indicate that blackwater fever may follow a very slight infection of malaria, and that the severity of the attack need necessarily bear no relation to the severity of the hemoglobinuria.

It would appear that to base a belief in the causative relation of previous malarial infection to hemoglobinuric fever on the finding of a few grains of malarial pigment at autopsy in individuals residing in a malarial locality such as the Isthmus of Panama, where Whipple made his investigations, is hardly warranted, for in most patients dying of any disease in such regions, the organs would undoubtedly show a few grains of malarial pigment. If, in such a case, death were due to yellow fever, it would hardly be justifiable to assert that the malarial pigment present proved that the disease was of malarial origin. As I have stated, numerous cases of hemoglobinuric fever are on record, in which, even at autopsy, both parasites and malarial pigment were absent from the blood and tissues. Major Walter D. Webb, Medical Corps, United States Army, retired, has recently handed me the notes of two cases of hemoglobinuric fever, observed by him, in which neither on the first day of the attack, nor at autopsy, could malarial pigment or parasites be found in the blood or in scrapings from the spleen or liver. In both of these cases the onset was sudden, while the individuals were in apparent health, and in one of the cases the patient stated that he had never suffered from malarial fever. The argument that in such cases as these the malarial infection may have been latent, is negatived by the fact that at autopsy the organs presented no evidence of malarial infection, and it is impossible for one to believe that this would be so had the patients suffered from latent malaria. In one of Webb's cases no quinin had been given before the attack.

The discordant results obtained by various observers as to the occurrence of malarial plasmodia in patients suffering from hemoglobinuric fever, and the proportion of patients showing the plasmodia before or during the attack, is very largely due to the fact that malarial infection is very much more prevalent in some blackwater fever regions than it is in others, and thus a much greater proportion of the inhabitants suffer from such infection. It appears to be most illogical to maintain that, because the plasmodia are found in a certain proportion of hemoglobinuric fever patients, the disease must be caused by these parasites, in view of the absolute proof that cases of the disease occur in which neither past nor present malarial infection has occurred. A single case of hemoglobinuric fever occurring in an individual who has never suffered from malarial infection, and in whom, even at autopsy, no trace of present or past infection can be demonstrated, should be enough to convince the most skeptical that malaria is not the cause of this disease, and many such cases are on record.

THE RELATION OF THE SPECIES OF MALARIAL PLASMODIA TO HEMOGLOBINURIC FEVER

A few authorities hold that hemoglobinuric fever is due to the estivo-autumnal plasmodia, or to a specific form hitherto undifferentiated. This theory is negatived by the fact that all species of malarial plasmodia have been found in the blood of patients suffering from this disease, and that the disease occurs in individuals in whom no plasmodia can be found either before, during, or after the attack of hemoglobinuria. It is, however, an accepted fact that the estivo-autumnal plasmodia are more frequently associated with hemoglobinuric fever than are the other species, but there are many cases reported in the literature in which the other species of plasmodia were found.

According to Deaderick,[21] the tertian plasmodium has been found in cases of hemoglobinuric fever by Ziemann, Panse, Orme, Pecori, Carducci, Van der Horst, Hughes, Koch (five cases), A. Plehn (three cases), Ollwig, McElroy, Goltman and Krauss, Brem, Herrick and Curl; while, according to the same authority, the quartan plasmodium has been found associated with this disease by Vincenzi, Grocco, Kleine, Kudicke, and Otto. These observations prove that, if this disease be due to malarial infection, it may be produced by any of the species of plasmodia, and that the more frequent occurrence of the estivo-autumnal plasmodia does not prove them to be the cause of the disease, any more than the more frequent occurrence of these species of plasmodia in kala-azar patients proves them to be the cause of that disease.

As regards the presence of an undifferentiated species of malarial plasmodium, the fact that the disease occurs associated with all of the known species of plasmodia is conclusive proof that such a species is not necessary, and, in addition, all of the plasmodia associated with this disease have been very carefully studied by eminent authorities and have not been found to differ from those usually observed in malarial infection.

The theory that hemoglobinuric fever is merely one of the forms of pernicious malaria, which is held by many French and American observers, is negatived by the fact that this peculiar form of pernicious malaria occurs only in restricted localities, and that it is absent in many regions where the worst forms of pernicious malaria occur. Koch first thoroughly disproved this theory and anyone who cares to study the literature will become convinced that it is untenable in the face of the evidence that has accumulated against it.

CHANGES IN THE BLOOD IN HEMOGLOBINURIC FEVER

The blood examination in patients suffering from hemoglobinuric fever generally demonstrates an increase in the large mononuclear leukocytes, and frequently the presence of pigmented leukocytes. The increase in the large mononuclear cells has been used as a weighty argument in favor of the malarial nature of the disease, but it is perhaps the weakest of all the arguments used by the advocates of this theory. While an increase in these cells occurs in both malaria and hemoglobinuric fever, a similar increase is more or less characteristic of other acute infectious diseases, and occurs almost constantly in sleeping-sickness, kala-azar, and recurrent fever. The fact that an increase in these cells occurs in blackwater fever simply suggests that the disease may be caused by a protozoon, and is really a better argument for the specific theory than for the malarial theory.

The presence of pigmented leukocytes has little value, as they occur in the vast majority of individuals residing in intensely infected malarial localities, and sometimes persist for weeks after all other traces of malarial infection have disappeared. While the presence of pigmented leukocytes indicates that at some time the patient has suffered from malarial fever, it is very slender proof of the malarial nature of hemoglobinuric fever.

AUTOLYSIS AND THE PRODUCTION OF HEMOGLOBINURIC FEVER

Since the remarkable development of our knowledge regarding hemolytic phenomena, the theory that an autolysin is produced in the blood of certain individuals by repeated attacks of malaria, thus leading to the production of hemoglobinuria, has become a favorite one, and is held by many observers, notably Deaderick, Bignami, Cassagrandi, and Christophers and Bentley. None of the believers in this theory have been able to demonstrate conclusively the presence of an autolysin in the blood of patients suffering from hemoglobinuric fever, although every effort has been made to do so. The theory is disproved by the fact that this disease occurs in persons who have not suffered from repeated malarial attacks, and that autolysins have not been demonstrated in the blood of man either in health or disease.

Some of the theories regarding the production of this theoretical autolysin are very complicated, but they are all negatived by the recent work of several observers who have failed to find such a body in the blood of patients suffering from hemoglobinuric fever, or in that of patients suffering from other diseases. The work of Dudgeon and Wilson,[35] Moss,[36] and Barratt and Yorke,[23] is of great interest in this connection. Dudgeon and Wilson found that, while some samples of normal serum have the power of agglutinating almost all specimens of normal red corpuscles, in no case were they able to find auto-agglutination or autohemolysis in normal blood. In blood from disease they were unable to find a single instance of autohemolysis, even in twenty-one cases of pernicious anemia, in which, as they say: "of all diseases it might well be imagined that autohemolysis could be demonstrated, but a negative result was obtained in every instance."

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[35] Dudgeon, L. S., and Wilson, H. A. F.: On the Presence of Hemagglutinins, Hemopsonins and Hemolysins in the Blood Obtained from Infectious and Non-Infectious Diseases in Man, Quart. Jour. Med., 1910, iii, 285.

[36] Moss, W. L.: Studies on Iso-agglutinins and Isohemolysins, Bull. Johns Hopkins Hosp., 1910, xxi, 63.

The very thorough work of Moss demonstrates beyond question that autohemolysis does not occur in either health or disease, and it is a significant fact that he found no constant differences between the agglutinating and hemolyzing qualities of serum in health and disease, which one would expect to find did disease tend to bring about an unstable condition of the blood leading to autohemolysis. Moss did not observe auto-agglutination in any of the 213 individuals that he studied, while autohemolysis was observed but once, and of this instance he says: "In the latter case the hemolysis may have been due to extraneous causes." He found that all of the serums investigated contained an antihemolysin which protected the homologous corpuscles.

Barratt and Yorke, in their recent and conclusive experiments regarding hemolysis in hemoglobinuric fever, were not able to demonstrate an autolysin in any of twenty-one cases which they investigated, while, in the eleven cases they examined as to the presence of an isolysin, but one gave a positive result. They conclude:

> From these experiments the important conclusion follows that the mechanism of production of blackwater fever stands in an altogether different category from that of paroxysmal hemoglobinuria. The presence of hemolysin or of defect of antilysis, which is present in the latter case, is absent in blackwater fever, where, therefore, search must be made for other factors.

These authors examined the blood of two oxen suffering from Texas fever, and of two dogs suffering from piroplasmosis, and were unable to find an autolysin in the blood of any of them. This fact is significant as showing the probable relationship of these infections to hemoglobinuric fever, a relationship which has been noted by many investigators.

Whipple,[34] as the result of careful experiments, also reaches the conclusion that the blood of hemoglobinuric fever patients does not contain any hemolysin.

It will thus be seen that the presence of an autolysin in the blood in hemoglobinuric fever has been disproved, and, even were such a body present, the advocates of the malarial theory would still have to explain why malarial infection produced it in some localities and never produced it in others. In other words, the presence of such a body in the blood of hemoglobinuric fever patients would point toward its specific nature rather than toward the malarial theory.

2. *QUININ AND HEMOGLOBINURIC FEVER*

The theory that hemoglobinuric fever is due to quinin will be considered but briefly, as it is not strictly included in the subject for discussion. This theory endeavors to explain the etiology of the disease by assuming that, in certain individuals, the administration of quinin is followed by hemoglobinuria, or that this results if the drug is administered to one who has suffered from repeated malarial attacks. Veratas, a Greek physician, suggested this explanation of the disease in 1858, and in 1874, Tomaselli gave it his support. The theory is believed in by many authorities, especially by Koch, whose support was accepted for a while as almost conclusive proof of its truth. As a matter of fact, many instances of hemoglobinuric fever have been reported in individuals who had never taken quinin, while the theory that the long-continued use of the drug for malarial infection may produce the disease is negatived by the fact that thousands of individuals take quinin, at intervals, for years, and never develop the disease except in regions where hemoglobinuric fever is endemic.

The occurrence of the disease in patients who have never taken quinin has been reported by A. Plehn,[5] in twenty-two cases; Cardamatis,[14] in thirty-two cases; Shropshire,[37] in twenty-five cases; Seal,[38] in six cases, and by many other observers.

My experience among the Filipinos positively disproves this theory, for of the hundreds of cases of malarial fever which I studied among these people, most of whom had suffered for years, at intervals, from malaria, the administration of quinin was not followed in a single instance by hemoglobinuria.

In the thousands of cases of malaria I have observed in soldiers of the United States Army, all of them treated with large, and frequently, heroic doses of the drug, I have observed but two cases of hemoglobinuria following its use, and in both the symptomatology was very different from that of hemoglobinuric fever. In those instances in which hemoglobinuric fever occurs among the natives of an endemic region, and many instances of this kind are on record, in hardly a single case had quinin been administered before the attack, and this must be true of the occurrence of the disease in any region where the drug is not in use by the native race.

It must be remembered that this disease occurs in malarial localities and that those suffering from the prodromal symptoms almost always take quinin, believing that they are suffering from malaria, and thus the hemoglobinuria which follows is quite naturally considered as being due to the drug.

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[37] Shropshire, W.: Hemoglobinuric Fever, Its Causes and Treatment, with Especial Reference to the Use of Quinin, Jour. Am. Med. Assn., 1903, xli, 600.

[38] Seal, C. E. B.: Notes on a Few Cases of Hemoglobinuria in India, Jour. Trop. Med., 1899, i, 179.

It is true that quinin does produce hemoglobinuria in some individuals, but in such instances the symptoms following each administration of the drug may occur in regions in which hemoglobinuric fever is unknown, and differ very much from the classical symptoms of hemoglobinuric fever. These cases should not be used as an argument in favor of the etiological relationship of quinin to this disease.

If quinin be the cause of this disease, it would be expected that the administration of it to patients suffering from an attack would result in an increase in the intensity of the symptoms and that death would follow in the majority of the cases. This is not so, however, for there is undisputed evidence that the mortality is very little higher when quinin is administered than when it is not. Deaderick[39] says:

> The great majority of cases recover even under the continued use of large doses of quinin.

It is also true that the severity of an attack of hemoglobinuric fever bears no relation to the size of the doses of quinin that have been administered, nor do large doses given during the attack result in a greater percentage of deaths than small ones. Shropshire[40] reports sixty-one cases treated with less than 5 grains per day, with 26.2 per cent. mortality; while in 141 cases treated with over 20 grains per day, the mortality was only 16.9 per cent. Crosse[41] states that in his experience the administration of the drug does not aggravate the attack, and that on the Niger all hemoglobinuric fever patients are treated with quinin and a large percentage recover. Moffatt[42] details six cases in which from 60 to 120 grains of quinin were given daily and all the patients recovered; while Robson[43] has given 60 grains of the drug at a single dose with good results.

Some authorities believe that quinin produces the disease only in certain individuals having an idiosyncrasy to the drug; but if this be true, we must believe that such idiosyncrasy occurs only in certain localities, for the drug is given in large doses, for long periods of time, all over the world, but hemoglobinuric fever only occurs in limited localities.

Barratt and Yorke[23] in their recent work on the mechanism of blackwater fever reach the following conclusions regarding the effect of quinin on the blood:

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[39] Deaderick, W. H.: A Practical Study of Malaria, Philadelphia, 1910, Ed. 1, p. 165.

[40] Shropshire: Med. Rec., 1903, lxiii, 798.

[41] Crosse: Blackwater Fever, London, 1899, Ed. 1.

[42] Moffatt: Brit. Med. Jour., 1898, i, 926.

[43] Robson: Brit. Med. Jour., 1898, i, 1287.

Owing to the toxicity of quinin, its concentration in the blood cannot reach an amount sufficient to allow of its direct hemolytic action on the red cells taking place during life. The red cells during blackwater fever are not hemolyzed by quinin bihydrochlorid more readily than in health.

Again, some authorities believe that hemoglobinuric fever is produced by quinin only when a person who has been taking the drug for a long time suddenly ceases to take it, and then takes a very large dose. This is disproved by the fact that this method of taking quinin is common throughout the world, while hemoglobinuric fever is restricted in its distribution; also by the fact that the disease occurs in individuals who have never taken the drug.

From this summary of the evidence against the quinin theory of the etiology of hemoglobinuric fever I believe that it is evident that quinin *per se* is not the cause of the disease. The facts that the drug is given throughout the world in large doses to individuals suffering from malarial infections, while hemoglobinuric fever occurs only in restricted localities; that many patients suffering from the disease recover under the administration of the drug; that patients who have apparently suffered from hemoglobinuria produced by quinin do not generally relapse when the drug is given; that there exists no relation between the amount of quinin given and the severity of the disease; that the disease occurs in individuals who have never taken quinin; and that the red blood-corpuscles of patients suffering from hemoglobinuric fever are as resistant to the drug as are the red cells of the normal individual, all point conclusively to the opinion that quinin cannot be regarded as the cause of hemoglobinuric fever.

3. THE SPECIFIC THEORY OF THE ETIOLOGY OF HEMOGLOBINURIC FEVER

PRESENT STATUS OF THEORY

From the evidence which has accumulated regarding the relationship of malaria and quinin to hemoglobinuric fever, it would appear that we cannot with justice regard either as being the etiological factor in the production of the disease, and that, therefore, we must consider the etiology of this disease as still undecided. This being so, it is but natural that many authorities have endeavored to prove that hemoglobinuric fever is a distinct disease due to a specific organism, and it must be admitted, that there is much evidence which points to such a conclusion. As early as 1892, Manson,[44] in an address delivered before the Epidemiological Society of London, stated that he believed hemoglobinuric fever to be a distinct disease; but it is chiefly to Sambon that we owe the awakened interest in the specific theory of the disease. In two excellent papers[45] this author has called attention to the inadequacy of the malarial and quinin theories and collected the evidence in favor of the specific nature of the disease. At the present time this theory is steadily gaining ground, its most ardent advocates being Manson, Sambon, Rho and Blanchard, while numerous other investigators concede that only by admitting the specific nature of the disease can the contradictions inherent in the other theories be explained. Every evidence which has been urged for the malarial nature of the disease can be used as well in advocating its specific nature, and, in adidtion, there are certain positive facts which can be accounted for only by admitting that the disease is due to some hitherto undescribed parasite.

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[44] Manson, Sir Patrick: Tr. Epidemiol. Soc., 1892-1893, xii, 384.

GEOGRAPHICAL DISTRIBUTION

As I have already pointed out, the geographical distribution of this disease is a much stronger argument for its specific nature than for the malarial theory. The fact that the disease occurs only in malarial localities simply proves that the parasite causing it finds in such localities the conditions necessary for its development or transmission, and the limited distribution of the disease in even the most malarial localities speaks still more strongly for its specific nature. The geographical distribution of kala-azar is very like that of hemoglobinuric fever, so far as its limitation to certain districts is concerned, and the latter disease, so far as I know, also occurs only in malarial localities. There are other acute infectious diseases which are still more limited as regards distribution, for instance, Rocky Mountain spotted fever, which occurs only in very restricted localities in our own country, and the tsutsugamushi disease, or flood fever of Japan, which occurs only in certain small districts along the course of rivers in northern Japan. Sleeping-sickness is another disease which occurs only in malarial localities, but we do not believe, because of its geographical distribution, that it is due to malaria.

The fact that the disease occurs in patients who have never suffered from malaria or taken quinin, and in whom, even at autopsy, no trace of past or present malarial infection can be demonstrated, is positive proof that it is not due to either of these factors, and speaks in favor of its specific nature.

The occurrence in the endemic regions of hemoglobinuric fever of certain small areas, and of certain houses in which the disease is most frequently observed, points very strongly to a specific cause and probably indicates that in such places there exist certain factors which enable the disease to be transmitted. It is evident that hemoglobinuric fever is a comparatively rare disease, even in its endemic centers, and this fact again points to its specific nature, rather than to its being due to malaria, and indicates that the cause is some parasite which requires very particular conditions either for development or for transmission.

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[45] Sambon, L. W.: Blackwater Fever, Jour. Trop. Med., 1898, i, 70; The Etiology and Treatment of Blackwater Fever, Jour. Trop. Med., 1899, i, 243, 262, 295.

DISPROPORTION BETWEEN NUMBER OF MALARIAL AND HEMOGLOBINURIC FEVER CASES

The numerical disproportion between the cases of hemoglobinuric fever and of malaria, in even the worst endemic regions of the former, is a strong argument in favor of the distinct nature of this disease. No one will deny that the number of cases of hemoglobinuric fever occurring in any locality when compared with the number of malarial infections is very small; while in many regions hemoglobinuric fever is unknown, although thousands of cases of malaria occur every year. In Greece, Pampoukis observed 34,937 cases of malaria, of which only 0.7 per cent. presented hemoglobinuria; Burot and Lagrand[46] observed 559 fatal cases of malaria, and only five of hemoglobinuric fever; and Stalkarrt[18] observed many cases of severe malarial infection without seeing a case of hemoglobinuria. There are many localities in which hundreds of cases of malaria occur yearly and yet hemoglobinuric fever is so rare as to be regarded as a medical curiosity. The army statistics regarding this question are of the greatest interest and value. It should be remembered that these statistics deal with soldiers recruited from every portion of our country, and include men who have served in the United States, in Cuba, Porto Rico, and the Philippines. Table 4, compiled from the Reports of the Surgeon General of the Army, shows the number of admissions to army hospitals from malaria and hemoglobinuric fever from 1903 to 1908 inclusive.

TABLE 4.—MALARIA AND HEMOGLOBINURIC FEVER IN THE UNITED STATES ARMY FROM 1903 TO 1908, INCLUSIVE

	Admissions for — Entire Army —		Admissions for U. S., Cuba, Hawaii, Porto Rico and Alaska		Admissions for —— Philippines ——	
Year.	Malaria.	Hemoglobinuric Fever.	Malaria.	Hemoglobinuric Fever.	Malaria.*	Hemoglobinuric Fever.
1903......	13,608	0	2,685	0	10,923	0
1904......	4,955	0	2,170	0	2,785	0
1905......	4,833	2	1,942	1	2,891	1
1906......	6,077	3	2,042	1	3,766	2
1907......	3,395	1	1,280	1	1,963	0
1908......	3,030	0	1,424	0	1,484	0
Totals ..	35,898	6	11,543	3	23,812	3

* Of the 23,812 admissions from malaria in the Philippines at least 11,000 were due to the estivo-autumnal plasmodia.

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[46] Burot and Lagrand: Cited by F. Plehn, Tropenhygiene, Jena, 1906, Ed. 1.

It will be seen from Table 4 that, during the six years which it covers, there were 35,898 admissions from malaria in the entire army, and only six admissions from hemoglobinuric fever, while the fact that hemoglobinuric fever does not occur among the Filipinos, although malaria is a very common and severe disease among these people, is well shown in Table 5, which gives the number of admissions from malarial fever and hemoglobinuric fever, from 1903 to 1908, inclusive, in the Philippine Scouts, an organization composed of native Filipinos from all parts of the Islands.

TABLE 5.—MALARIA AND HEMOGLOBINURIC FEVER IN THE PHILIPPINE SCOUTS FROM 1903 TO 1908, INCLUSIVE

Year.	Admissions from Malaria.	Admissions from Hemoglobinuric Fever.
1903	2,565	0
1904	1,691	0
1905	2,710	0
1906	1,871	0
1907	1,463	0
1908	1,205	0
Totals	11,505	0

From the above table it is seen that while there were 11,505 admissions from malarial fever among the Philippine Scouts during the six years mentioned, there was not a single admission from hemoglobinuric fever. If these figures are added to those for our army, exclusive of the scouts, there are 47,403 admissions from malarial fever with but six admissions from hemoglobinuric fever, or 0.00012 per cent.

In my own experience, covering over ten years' observation of the malarial fevers, during which time I have had the opportunity of studying nearly 6,000 cases of malaria in which the plasmodia were demonstrated in the blood, I have observed only two cases of hemoglobinuria, and in both of these the symptoms were not typical of true hemoglobinuric fever. All of the malarial cases were observed in Cuba or the Philippines, or in the United States in soldiers returning from service in these countries, and almost every one of them had suffered from repeated attacks of malarial fever, fully two-thirds of them from estivo-autumnal infections. In view of these facts, is it possible to believe that hemoglobinuric fever is due to malarial infection? It appears to me that this great disproportion between the number of cases of malaria and hemoglobinuric fever is very strong proof of the specific nature of the latter disease.

OCCURRENCE IN EPIDEMICS

The occurrence of epidemics of hemoglobinuric fever is proof of its specific nature. While there are many instances of the occurrence of epidemics of malarial fever, there are no instances of epidemics of a special symptom-complex associated with this disease, and this is what hemoglobinuric fever is believed to be by the advocates of the malarial theory. Epidemics of this disease have been reported by various observers. Sambon[13] recalls the epidemic which occurred among the laborers on the Isthmus of Corinth, and the Chinese laborers on the Congo railway; and the same disease has occurred in epidmic form on the Isthmus of Panama during the French operations on the canal. According to Dr. Wenyon[47] the disease ravaged like a plague the Chinese army on the Tonquin border of Kwansi, and the same authority instances an outbreak in a prison in Sardinia, in which twenty-four out of 800 convicts suffered from the disease. According to A. Plehn,[48] hemoglobinuric fever not infrequently occurs in epidemic form in Africa, and he mentions several such instances. In this relation may be mentioned the instances already quoted, in which several individuals in the same house develop the disease, although those living in the surrounding buildings do not suffer.

The fact that hemoglobinuric fever occurs in regions where the natives are immune to malaria is an argument for the specific nature of the disease. We are informed on the authority of A. Plehn that the negro of Africa is not immune to hemoglobinuric fever; and Doering,[49] F. Plehn,[50] and others have observed cases among the negroes of that country. It is generally accepted as proved by the researches of Koch and others that the natives of certain malarial regions in Africa, after reaching adult life, are immune to malaria, and Koch did not find the plasmodia in 100 per cent. of the adult natives whom he examined. How can we reconcile these two facts, if hemoglobinuric fever be due to malarial infection? Is it not more reasonable to believe that we are dealing with a distinct disease, due to a specific parasite?

SYMPTOMATOLOGY AND PATHOLOGY

The symptomatology of hemoglobinuric fever is distinctive and unlike that of any form of malarial fever with which we are acquainted. The lack of periodicity in the temperature curve, the presence of an enlarged and tender liver, the repeated chills, the occurrence of marked jaundice, the leukocytosis, and the hemoglobinuria, have all been instanced by Sambon[13] and other authorities, as definitely separating the disease on clinical grounds from malarial fever. The fact that, in relapses of this disease, the symptom of hemoglobinuria is always repeated proves that we are not dealing with a pernicious form of malaria, for relapses of pernicious malaria are not always accompanied by the same

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47. Wenyon: Cited by Sambon, The Etiology and Treatment of Blackwater Fever, Jour. Trop. Med., 1899, i, 243, 262, 295.

48. Plehn, A.: The Cause, Prevention and Treatment of Hemoglobinuric Fever in Warm Countries, Jour. Trop. Med. and Hyg., 1908, xi, 294.

49. Doering: Cited by Deaderick, A Practical Study of Malaria.

50. Plehn, F.: Arch. f. Schiffs. u. Tropen. Hyg., 1904, iii, 336.

symptoms. While the prodromal symptoms of hemoglobinuric fever cannot be differentiated from those of malaria, the symptoms of the fully developed attack are distinctive.

The pathologic changes in hemoglobinuric fever is very strong proof of its specific nature, for the lesions are not those of pernicious malarial fever. Even the most ardent advocates of the malarial hypothesis admit that cases occur in which not even a few grains of malarial pigment can be found in the viscera, and there is no evidence of either present or past malarial infection. It is generally conceded that, unless the lesions of a disease are found at autopsy, it is not justifiable to believe the cause of death to be due to that disease, and it would appear that it is fully justifiable to disregard the malarial theory of hemoglobinuric fever because of the pathological lesions present in fatal cases. The absence of malarial pigment or parasites in the organs, or in the blood in many cases, the condition of the kidneys, which is seldom simulated in pernicious malaria, the enlarged, but unpigmented liver and spleen, are all very different from the lesions usually observed in fatal malarial infections. The enlargement of the spleen in uncomplicated cases of hemoglobinuric fever is exactly similar to that occurring in most infectious diseases, and is no proof of its malarial origin. One would think that, after the disastrous experience regarding the significance of splenic enlargement in kala-azar, it would not again be urged as an argument for the malarial etiology of any disease, but in the case of hemoglobinuric fever it is still so used. In his study of the pathology of this fever Whipple[34] gives very completely the lesions he found in nine cases of this disease, lesions which are certainly not those encountered in the vast majority of fatal cases of malarial fever. He calls attention especially to the occurrence of extensive areas of necrosis in the viscera, especially the spleen, and, while small areas of focal necrosis are sometimes found in the spleen, liver, and other organs in pernicious malaria, they are not peculiar to malarial infections, but occur also in diphtheria, streptococcus septicemia, and other acute infections in which a toxemic condition is present. The fact that they are much more pronounced in hemoglobinuric fever would appear to prove that the etiology of this disease is not that of malarial infection.

The occurrence of necrosis of the Malpighian bodies of the spleen. spoken of by Whipple, and which, according to this author, involves almost every Malpighian body in that organ, is never found in malarial infections in my experience, and alone serves to differentiate that disease from any form of such infection. It is impossible to read Whipple's excellent account of the pathology of hemoglobinuric fever without concluding that it is not due to malarial infection, for, while the two conditions have some things in common from a pathological standpoint, the pathology of other tropical infections, such as yellow fever and kala-azar, have as much in common with malaria as does this disease. The presence of a small amount of malarial pigment cannot be held as proving the etiological importance of malarial infection, for the same pigment is found in patients dying of other diseases in malarial localities, and, as has already been shown, many cases are on record in which at autopsy no pigment could be found.

APPARENT ABSENCE OF PARASITE

One of the arguments brought forward against the specific theory of the origin of hemoglobinuric fever is the fact that, although it has been carefully searched for, no one has been able to demonstrate a parasite which could be considered as being the cause of the disease. I am sure that all will agree with me when I say that such an argument is valueless. There are a number of infections in which the cause has not as yet been demonstrated, yet one never uses this argument as valid evidence against their specific nature. Yellow fever, dengue, Rocky Mountain spotted fever and nearly all of the eruptive fevers belong in this category, and I believe that further research will show that many of these diseases are caused by a class of organisms very closely related and probably of protozoan nature.

There are many explanations for the apparent absence of a parasite from the blood and tissues in hemoglobinuric fever, among which may be mentioned a possible cyclical appearance of the parasite in the blood; the small number in the blood at any one time; the location of the parasite in some internal organ from which it rapidly disappears after the death of the patient; and the fact that the organism may be ultramicroscopical in size. The recent researches of Miyajima[52] on a piroplasma found in the blood of cattle in Japan, and of Crawley[53] on a trypanosome occurring in the blood of our own cattle, are of interest and significance in this relation. Both of these organisms occur in such small numbers in the blood of their respective hosts that they cannot be demonstrated in that fluid with the microscope, but, if the blood be added to suitable culture media, it is possible to secure the organism in pure culture. The same may be true of hemoglobinuric fever. The parasite may be present in such small numbers that a microscopic examination of the blood will not reveal it, but cultural methods might result in success. Curiously enough, I can find no record in the literature of an endeavor to make blood cultures in this disease.

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52. Miyajima, M.: On the Cultivation of a Bovine Piroplasma, Philippine Jour. Sc. B. Med. Sc., v, 83.

53. Crawley, H.: *Trypanosoma americanum*, N. Sp., A Trypanosome which Appears in Cultures Made from the Blood of American Cattle, Bull. 119, Bureau of Animal Industry, Dept. Agri., Washington, 1909.

CONCLUSIONS

That hemoglobinuric fever is not due to malaria I believe to be proved by its geographical distribution; by the fact that it occurs in individuals who have never suffered from malaria; and by the fact that, in many instances, neither before, during, or after an attack can plasmodia be demonstrated in the blood, while, even at autopsy, no trace of malaria can be found.

That the disease is not due to quinin is proved by the fact that it occurs in individuals who have never taken the drug, and that in many regions where the drug is extensively used the disease is unknown.

For the following reasons I believe that it is due to a specific organism: its geographical distribution; its numerical disproportion to malaria wherever it occurs; its occurrence in epidemics; the character of the pathological lesions; its symptomatology; the lack of conclusive evidence that it is due to malaria; and its analogy with other well-known infectious diseases.

In concluding I desire to call attention to the peculiar relation that this disease apparently bears to the hemoglobinuric fever of cattle and to piroplasma infections in general. That hemoglobinuric fever resembles Texas fever in its symptomatology has often been noted, and there is much reason to believe that it may be due to a similar parasite, for it is a significant fact that some form of piroplasma infection has been observed in almost every region in which blackwater fever is endemic. That no piroplasma has as yet been demonstrated in the blood in this disease does not count for anything, for it may be so small as to be indistinguishable by our present lenses, or it may occur in such small numbers as to necessitate its demonstration by cultural methods. All of the parasites belonging to this class are very minute and it is not at all improbable that the parasite of hemoglobinuric fever is ultramicroscopical in size, as we believe the parasites of yellow fever, dengue, and other diseases to be. Hemoglobinuric fever is probably transmitted by an insect, perhaps a larval tick, as is the case in tsutsugamushi disease, or the adult insect, as in Rocky Mountain spotted fever; but, whatever insect is ultimately proved to be the transmitting agent, we may feel sure that it will be one of comparatively rare occurrence, or that the conditions necessary for the transmission of the disease are peculiar, either in the cycle of development of the parasite in its insect host, or in the manner in which it reaches the insect. Only in some such manner can the comparative rarity of the disease in regions in which it is endemic, and its absence from others, be explained.

I would also call attention to the extremely small number of experiments which have been made on animals in research work on this disease. It is most unfortunate that the majority of investigators who have worked on the etiology of hemoglobinuric fever have been strongly biased in favor of either the malarial or quinin theories, and have not considered animal experimentation necessary in solving the problem. That such experimental methods are of the greatest value in medical research, and absolutely indispensable, if our work is to be crowned with success, has been well shown by the results which have recently been accomplished in the study of dengue, typhus fever, Rocky Mountain spotted fever, and acute poliomyelitis.

Let us attack the problem of the etiology of this disease in a similar manner and I believe that it will not be long before we shall be able to prove beyond question that hemoglobinuric fever is a disease *sui generis* and not a manifestation of malaria.

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THE PATHOLOGY OF BLACK-WATER FEVER.*

By G. H. Whipple, M. D., Baltimore.

A careful report covering the substance of this paper has appeared during the past year and for all details and discussion reference can be made to that publication.** The material obtained for study was derived from the Ancon Hospital Laboratory, Panama, during a year's work in that laboratory, 1907 and 1908. In the study of many cases it was found that there are two pretty distinct groups in which haemoglobinuria may be present:

1. The typical paroxysmal cases of black-water fever, in which there are very few or no malarial parasites demonstrable in the circulating blood.
2. Cases of pernicious malaria in which there may be a little or no haemoglobinuria but the circulating blood is loaded with malarial parasites.

All gradations between these two extremes were studied and reported in our series of cases. We may summarize the pathological picture in black-water fever somewhat as follows:

The **kidneys** in haemoglobinuria are usually a little enlarged; the surface deep red or mottled red and yellow; the cortex swollen and stippled with red or black dots. The organ may have a yellow or even a greenish tint if the jaundice is extreme. If acute nephritis has supervened the cortex may be swollen and œdematous. Acute nephritis is not a constant finding. Five cases out of nine showed no sign of injury from the presence of much haemoglobin in the tubules. Three cases of pernicious malaria with black-water presented no evidence of acute nephritis. The kidneys of pernicious malaria are usually normal except for a little pigmentation, but acute nephritis may be present here as well.

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* Read at the seventh annual meeting of the American Society of Tropical Medicine, June 11, 1910.

**"Black-water Fever and Pernicious Malaria in Panama." Malaria Bd. 1-H-4-S. 215-1909.

Reprinted from Gulf States Journal of Medicine and Surgery and Journal of the Southern Medical Association, September, 1910.

The **spleen** shows many interesting changes, many of which may be associated with any profound toxaemia; for example, diphtheria, septicæmia and typhoid fever. The spleen is invariably enlarged, weighing from 180 to 1,250 grams. In black-water fever the organ presents a purplish, velvety pulp and very opaque, sharply outlined Malpighian bodies. It is usually friable. In pernicious malaria the spleen pulp is of a dark chocolate color in acute cases, of a slaty color in the more chronic cases, and the Malpighian bodies are inconspicuous. **Necrosis** may be the striking feature of the microscopical picture of black-water fever, and in acute cases may involve a great part of the pulp and Malpighian bodies. Malarial pigment may be scarce or abundant, but always present. The Malpighian bodies in a great majority of cases present a central necrosis. This necrosis may involve a small part or almost all of an entire follicle. Pernicious malaria may show these same necroses, but they are much less conspicuous. The lymphatic apparatus may show similar changes in the two diseases and resemble that described in the spleen except for the fact that the necrosis is less in evidence.

The **bonemarrow** is almost always hyperplastic, depending on the severity of the blood destruction. Hyperplasia was absent in one case of pernicious malaria. The marrow shows no evidence of a similar necrosis. The hyperplasia affects particularly the red corpuscle groups. There is distinct increase in eosinophile marrow cells. This is noted in smears and microscopical sections from rib and femur. It is well known that eosinophiles are decreased in the circulating blood, and this may be explained by their retention in the bonemarrow, perhaps due to some specific stimulus.

The **liver** is usually enlarged, and the color varies from a pale chestnut brown or bronze to a greenish or slaty color, depending upon the amount of jaundice and malarial pigment. The gall bladder in cases of black-water fever is filled with a characteristic dry, curdy and finely granular black bile. Focal necroses are rare in pernicious malaria, but are common, and may be very striking in black-water fever.

The brain in black-water fever is very pale and waxy looking, while in pernicious malaria it may present a characteristic appearance: a deep rose pink or a pale, slaty coloration, some times speckled with tiny ecchymoses.

The other organs show no changes of importance.

Examination of smears from marrow, spleen and liver show malarial pigment in small or large amounts to be an invariable finding.

The two diseases present many features in common, indicating some circulating poison in both diseases which is very similar in its action and very apt to attack the lymphatic apparatus. This unknown poison is surely more intense in black-water fever, as indicated by the amount of tissue necrosis, and runs a parallel course with the intensity of hæmolysis, which may or may not depend upon it.

From the study of these cases it is believed that the site of blood destruction is not any particular organ but that the solution of red blood cells takes place in the circulating blood just as the destruction of red blood cells by the malarial parasite takes place in all parts of the vascular system. Perhaps it may be safe to assert that black-water fever is malaria plus an unknown factor, possibly a poison that develops as the result of some reaction against the malarial parasite. No case of black-water fever has been reported in which careful search has not revealed evidence of a preceding malarial infection as indicated by more or less malarial pigment in the different viscera.

CLINICAL OBSERVATIONS ON HEMOGLOBINURIC FEVER.*

By William H. Deaderick, M. D., Helena, Arkansas.

Of the last 34 cases of hemoglobinuric fever which I have treated I have kept more or less complete histories. While all the cases occurred in private practice and about four-fifths of them in the country and among a class of people unaccustomed to record temperature, pulse and other clinical data a crude analysis may prove of interest.

The 34 cases were distributed by months as follows: July, 1 case; August, 4; September, 10; October, 12; November, 6; December, 0; January, 1.

Thirty cases occurred in whites and four in negroes, of whom two were blacks and two mulattoes.

Males were affected twenty times, females fourteen times. Two of the negroes were males and two were females.

Ages showed the following distribution:
6 to 10 years—12 cases.
11 to 15 years—9 cases.
16 to 20 years—2 cases.
21 to 30 years—2 cases.
31 to 40 years—4 cases.
41 to 50 years—3 cases.
51 to 60 years—2 cases.

Twenty-seven cases occurred among the farming class, two in a printer, two in town school children, and one each in a carpenter, a liveryman, and a teacher. Twenty-seven cases were seen in rural residents and seven in towns people.

Secondary etiological factors as alcoholism, cold and other influences were not prominent in these cases, though indigestion is recorded in one case and exposure to cold and rain in two cases.

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* Read at the seventh annual meeting of the American Society of Tropical Medicine, June 11, 1910.

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All without exception had suffered previously with malaria, most of them repeatedly. Nineteen cases occurred in malarial cachectics. Fourteen of the patients had previously had blackwater fever. Of this number seven had had one attack, three two attacks, and one each four, five, six and seven attacks. A case occurred in the practice of a colleague in which death took place in the eleventh attack.

In eleven instances other cases had occurred in members of the immediate family and three families appeared to show a very marked predisposition. Only once were members of the same family affected the same year, the interval between the dates of onset being 55 days.

In 30 cases quinine was being taken for malaria when the outbreak occurred. In four cases quinine could be absolutely excluded. The majority of those having taken quinine had taken the sulphate by mouth, one the bisulphate, and three had taken patent "chill-tonics." The smallest quantity was two grains of the sulphate.

Prodromata which were present in the majority of instances consisted of those of the ordinary malarial attack.

The mode of onset was with a chill in all cases but four. Two of these cases began with pain in the epigastric region, and in two the fever rose without chill, followed soon by a discharge of blackwater. In one case the chill and hemoglobinuria were simultaneous, but the average period between the chill and the first dark urine was two hours.

The temperature averaged from 100 3-5 to 102 4-5, the highest recorded being 104 1-2. It was continuous and remittent excepting in one instance, where it showed tertian intermittent periodicity. Estivoautumnal tertian parasites were found in the blood of this patient.

The pulse averaged from 110 to 135. It soon became soft and compressible and in severe cases small and feeble.

Respirations varied, according to the degree of fever and of blood destruction, from 30 to 60.

Of the four cardinal symptoms of blackwater fever, fever, hemoglobinuria, icterus and vomiting, the first two were present in all my cases. Jaundice, though not always present at the first visit, appeared later in all but one or two very mild attacks. Yellow scleræ were present in over half the cases, and in a number the discoloration was intense. Vomiting occurred in four-fifths of the cases and was very distressing in half the cases.

The bowels were regular, constipated or loose, depending in great measure on whether or not a purgative had been taken.

Singultus was observed in a majority of the fatal cases.

Though most of the patients were very miserable, pain was not a prominent feature in many of them. Pain in the head is recorded oftenest, next in the epigastrium, then in the back.

Herpes was not observed in a single case.

The liver was tender in half the cases, but was markedly enlarged only once.

There was tenderness over the right kidney in one patient.

The spleen was always enlarged, often extremely so, extending beyond the umbilicus and to the anterior superior spinous process. The enlargement was often rapidly progressive and the organ frequently tender.

The lungs were negative; the heart emitted a systolic murmur in about one-third of the cases.

The reaction of the urine was usually acid. The average of a large number of urinalyses gave a specific gravity of 1015. The average variation of albumin was from one-half to two and a half grams per litre estimated with the Esbach albuminometer, though specimens were observed containing five, six, seven, eight, nine, and two with fourteen grams per litre. In the last nine cases the urine was tested for quinine with negative results. Bile was found only once in the entire series, and then only in a moderate amount. Microscopically the most conspicuous finding was a dirty brownish granular detritus. Epithelia were numerous, round, spindle and squamous cells occurring in the order of frequency. Casts appeared sooner or later in every case; the granular were the most numerous, then the epithelial. Red blood cells were found in five of the 34 cases, only once in very large numbers.

The blood showed wide variation in hemoglobin content. One mild case ran its course with the hemoglobin not falling below 70 per cent. On the other hand a case ending fatally was seen in consultation in which the patient was practically exsanguinated. He had been treated actively with entoroclysis and hypodermoclysis and the fluid obtained by puncture of the lobe of the ear was straw colored. The cover glass adhered to the immersion lens rather than to the slide so that a dry lens had to be used for the examination. Only a few very pale red cells were to be seen in each field of the microscope. In the majority of cases the hemoglobin fell to about 50 per cent. The lowest percentage observed in a case recovering was 30. The commonest variations shown by the red cells were polychromatophilia, macro- and microcytosis, and poikilocytosis, the former being the most common. It was surprising in many cases to see so few changes in the character of the red cells. A number of differential leucocyte counts give the following average proportions: small mononuclears 12 per cent., large mononuclears 35 per cent., polymorphonuclears 52 per cent., eosinophiles 1 per cent. In the 34 cases parasites were found in 14, while the examination was negative in 20. The blood examinations were made for the first time from the first to the third days of the disease. In every instance in which parasites were found they were of the estivo-autumnal variety and differed in no way from the parasites occurring in the ordinary estivo-autumnal infections of this region.

With the exception of three unusually protracted cases the average duration of the fever in the 34 cases was 80 hours; the minimum was 12 hours. The fever in the three cases mentioned lasted 12, 19 and 28 days and was remittent. The blackwater in these cases continued 48 hours, 48 hours, and about 72 hours respectively. All three patients recovered. The average duration of the hemoglobinuria in the series was 50 hours, minimum 18 hours, and maximum 96 hours. In two cases the blackwater outlasted the fever, 96; 48 hours, and 18 1-2 hours.

There were remarkably few complications exhibited, in fact, only two, and these occurred in the same patient in different attacks. These were acute tonsilitis and otitis media not proceeded to suppuration. I know of two cases in pregnant women in the practice of two colleagues. Miscarriage occurred in both and both mothers died. One patient had purpura.

In two of my cases relapse occurred. In one the hemoglobinuria had continued 48 hours, the fever four days, the relapse occurred on the seventh day and lasted 12 hours. In the other the blackwater had continued 60 hours and the fever five days; the relapse took place on the sixth day and lastened only a few hours. These relapses were similar in onset and symptoms to ordinary attacks.

The only sequelæ that I encountered were cachexia and renal lesions. In exactly half the cases that I have been able to examine from a few months to several years since the attack abnormalities of the urine have been found. These consisted of albumin, cylindroids or casts. In only two or three were symptoms present which might be referred to a kidney lesion.

The diagnosis of all my cases was made immediately excepting in one instance. The patient, with an alcoholic history, had recently been exposed to cold and unusual exertion; backache was intense and the urine contained so many red blood cells that for a few hours I was in doubt as to whether he had a true hematuria or a hemoglobinuria. Another case, one of estivo-autumnal malaria, was seen in which the urine was so loaded with bile pigment that until it was examined chemically the case appeared to be blackwater fever.

Bad prognostic signs were marked diminution in the amount of urine, excessive and uncontrollable vomiting, somnolence, coma and singultus. This last symptom occurred in a majority of my fatal cases and was not seen in any patient who recovered.

Among the 34 cases there occurred 10 deaths. This high mortality may partially be accounted for by the fact that five of the fatal cases were seen in consultation, being unusually severe cases. Of the 10 deaths there were two deaths from suppression and eight from exhaustion. Three deaths occurred at the end of the second day, two during the third day, and one each on the fourth, fifth, sixth, seventh and eighth days. The two deaths from suppression took place on the third and seventh days. Two of the deaths occurred in negroes and eight in whites. Seven were males and three were females. From 5 to 10 years of age there was 1; from 11 to 20, three; 21 to 30, one; 31 to 40, three, and from 51 to 60, two. Five of the fatal cases were in persons who were cachectics at onset and five were in persons who were not cachectics. My experience has been that first attacks are the most fatal, eight of the ten deaths terminating first attacks, and two second attacks. One death occurred in July, two in August, two in September, three in October, and two in November.

Studies of Malaria in Panama. II. Treatment of Blackwater Fever

PERNICIOUS MALARIA WITH HEMOGLOBINURIA AND ERYTHROLYTIC HEMOGLOBINURIA

WALTER BREM, M.D.
COLON HOSPITAL, CRISTOBAL, CANAL ZONE

STUDIES OF MALARIA IN PANAMA. II. TREATMENT OF BLACKWATER FEVER

PERNICIOUS MALARIA WITH HEMOGLOBINURIA AND ERYTHROLYTIC HEMOGLOBINURIA*

WALTER BREM, M.D.
COLON HOSPITAL, CRISTOBAL, CANAL ZONE

"Blackwater fever" is a term commonly used to designate fever with hemoglobinuria, associated more or less definitely with malaria. It embraces, I believe, two types of hemoglobinuria, which should be clearly differentiated for purposes of treatment and of study. The first type is associated with enormous numbers of malarial organisms, and, like the hemoglobinuria of piroplasmosis, its intensity is in direct relation to the severity of the infection. The mechanism of its production is, I am led to believe, the immediate destruction of erythrocytes by segmenting parasites, and differs from the mechanism of the second type, which is due, it is generally conceded, to the solution of erythrocytes by an unknown hemolysin (erythrolysis). I venture to propose, therefore, that the terms "blackwater fever," "malarial hemoglobinuria," "hemoglobinuric fever," etc., be abandoned as leading to confusion and possibly to grave errors in treatment, and that the two types of hemoglobinuria be described under a differential nomenclature.

Type 1.—Pernicious malarial fever with hemoglobinuria. The etiology is known and it is better that the condition or symptom of hemoglobinuria should not receive a more prominent place in the diagnosis.

Type 2.—Erythrolytic hemoglobinuria. Our knowledge of the etiology of this type is incomplete, and until an etiologic terminology can be rationally applied it would seem best to use one based on the mechanism of production, and on the most prominent feature of the symptom-complex.

If I may be permitted to do so, I shall employ this nomenclature.

PERNICIOUS MALARIAL FEVER WITH HEMOGLOBINURIA

A typical example of this type is presented in the case reports (Case 1, Chart 1). The hemoglobinuria was anticipated from the examination of blood about thirty-four hours before it appeared; 15.6 per cent. of red blood corpuscles in the peripheral blood were infected; the urine had the characteristic appearance of "blackwater."

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* Read at the seventh annual meeting of the American Society of Tropical Medicine, St. Louis, June 11, 1910.

Since my attention was drawn to the separation of this type of hemoglobinuria, eight patients with pernicious malaria have been admitted to the hospital, and in the urine of all we were able to demonstrate the presence of hemoglobin; in the last six the blood examination led us to suspect its imminence, and to foresee approximately the time of its onset.

The hemoglobinuria varies in degree from traces of hemoglobin in the sediment discernible only by special tests to the intensity of "blackwater." Two of the eight patients mentioned voided typical "blackwater" urine; three voided urine recognizable by the eye as probably hemoglobinous; one passed reddish-brown urine with a suggestive grayish-brown sediment; the other two, urine that, to the eye, gave no suggestion of hemoglobin, which was demonstrable only in the sediment. The guaiac and turpentine test for hemoglobin was employed. Controls were made by

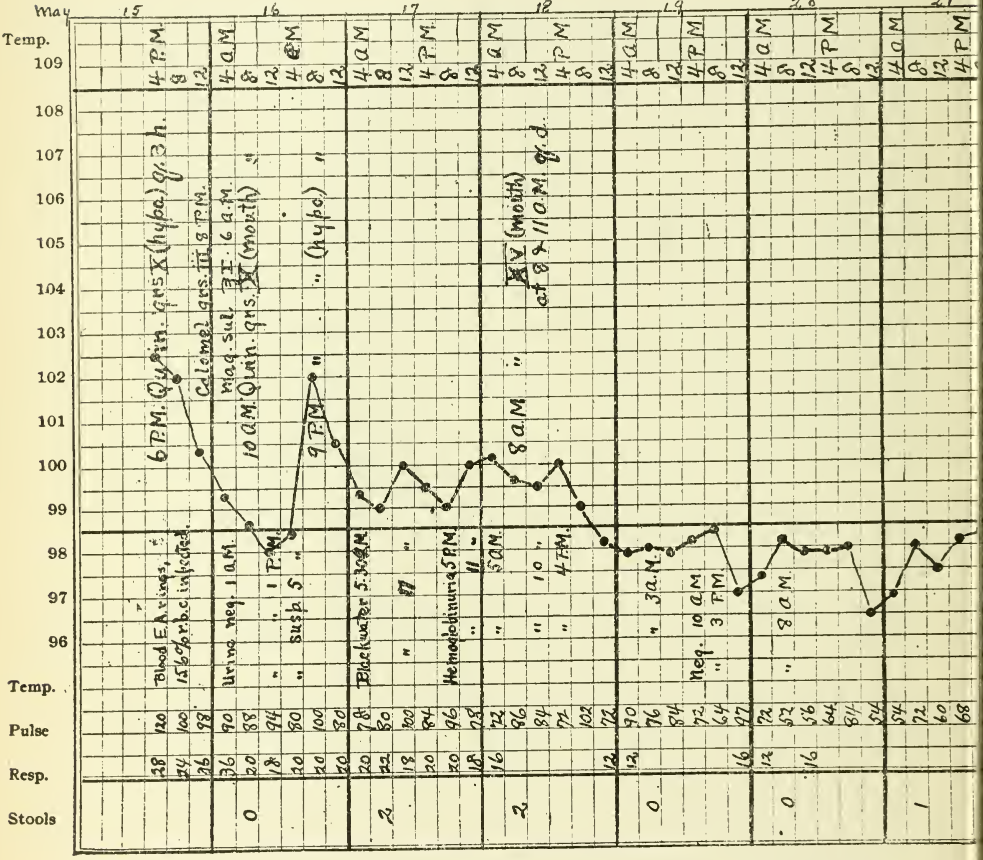

Chart 1.—Showing conditions in Case 1.—Pernicious malarial fever with hemoglobinuria.

testing the urine of hundreds of patients with mild or moderate malarial infections, and uniformly negative results were obtained. I feel confident, therefore, in saying that a positive reaction of the urine to the guaiac and turpentine test means the presence of hemoglobin.[1] Only a definite blue color was considered as indicating a positive reaction.

It is my belief at present that future examinations will demonstrate hemoglobinuria at some time during the course of every pernicious malarial infection. In some of the cases an examination of each specimen voided must be made, the urine must be sedimented, preferably in a conical glass, and the sediment used in the test for hemoglobin. If this belief proves to be well founded, the mortality of this type will be the mortality of pernicious malarial fever. Of my eight patients, one died from the malarial infection, the capillaries of his brain being stuffed with parasites; another died, after his malarial infection was controlled, from a subsequent infection with an organism (isolated at autopsy from the spleen) apparently belonging to the typhoid-colon group, but possessing atypical fermenting properties (no malarial parasites were found in smears from the spleen, bone-marrow and brain); the other six made rapid recoveries. I have been able to recall four other cases and to find records of two more. One of the four was a fatal case seen in Baltimore in Osler's wards in the Johns Hopkins Hospital and mentioned by me in a former report.[2] Five of these six patients died. This mortality is very high, because the diagnosis was made from the gross appearance of the urine, and hemoglobinous urine of blackwater intensity occurs only in the most severe infections. Among twenty deaths that I have seen associated with blackwater, five of them, or 25 per cent., were due to pernicious malarial infections. It would seem, therefore, that a considerable percentage of deaths, heretofore reported as due to blackwater fever, were really due to pernicious malarial fever with hemoglobinuria, which fact has an important bearing on comparative mortality statistics under different systems of treatment. Among twelve cases of blackwater fever in Panama, reported by Whipple,[3] in a pathologic study, three appear to have been of this type, and Whipple separates them from the ordinary type by designating them as "pernicious malaria and blackwater fever." Whipple made the important observation that the pathology of these cases, and, also, of pernicious malaria without apparent hemoglobimuria does not differ esssentially from that of "blackwater fever." Whipple did not observe evidence of hemoglobinuria in five other cases of pernicious malaria reported in the same study. But the detection of a mild grade of hemoglobinuria by a microscopic examination of kidneys would be a difficult or impossible task, and, as Whipple points out, the differ-

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[1] The following modification of the guaiac-turpentine test has been developed in the clinical laboratory of Colon Hospital for the examination of urine: Place 3 to 5 c.c. of urine containing sediment in a test-tube, add a few drops of glacial acetic acid; after a moment add 1 to 2 c.c. of ether and agitate gently, then a pinch of powdered guaiac resin, and lastly 10 to 20 drops of old turpentine. A pale blue to a blue-black color indicates a positive reaction, which may take a few moments to develop. If the ether does not separate well, a few drops of alcohol will facilitate the separation. The blue color may be brought out and the test rendered more delicate in doubtful cases by the following procedure: To the ether-turpentine mixture add chloroform drop by drop until all of the resultant mixture, except a thin layer, has been sunk to the bottom. To the thin layer remaining at the top, add carefully two or three drops of alcohol, then a few drops more of old turpentine. If inadvertently all of the ether-turpentine mixture has been sunk by adding too much chloroform, the alcohol and turpentine may be added as before and then a few drops of the sunken mixture recovered with a small pipette and added to the top layer.

[2] Brem, W.: Malarial Hemoglobinuria, Jour. Am. Med. Assn., 1906, xlvii, 1896, 1992.

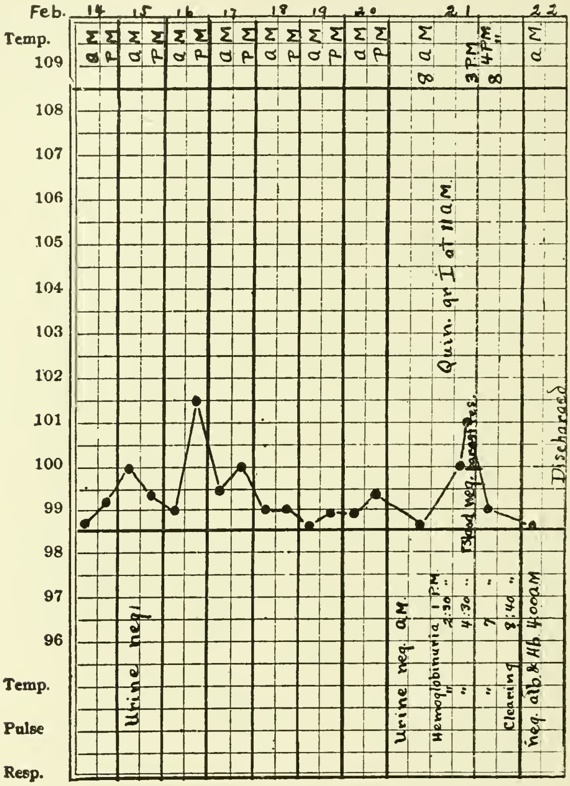

Chart 2.—No. 23,831. Patient, Frenchman, who had been on Isthmus six years, was admitted to Ancon hospital, Feb. 14, 1907. The patient had had several previous attacks of fever, "blackwater" being precipitated by quinin. The spleen was about 6 cm. below costal margin. The patient consented to take 1 grain of quinin as an experiment; blackwater followed in two hours. (Case from the clinic of Dr. A. B. Herrick, who kindly permits me to use it.)

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[3] Whipple, G. H.: Blackwater Fever and Pernicious Malaria in Panama, Malaria, Leipsic. 1909, i, 4, 215.

ence in the pathology is one of degree and not of kind. Moreover, the hemoglobinuria of pernicious malarial fever seems to be in proportion to the absolute number of parasites, and in treated cases these are always decimated by quinin in the general circulation, while death is usually produced by those blocking the capillaries of the brain. This is well illustrated by one of Whipple's cases (No. 1431). As a rule, then, when treated patients come to autopsy, the hemoglobinuria has almost or entirely disappeared.

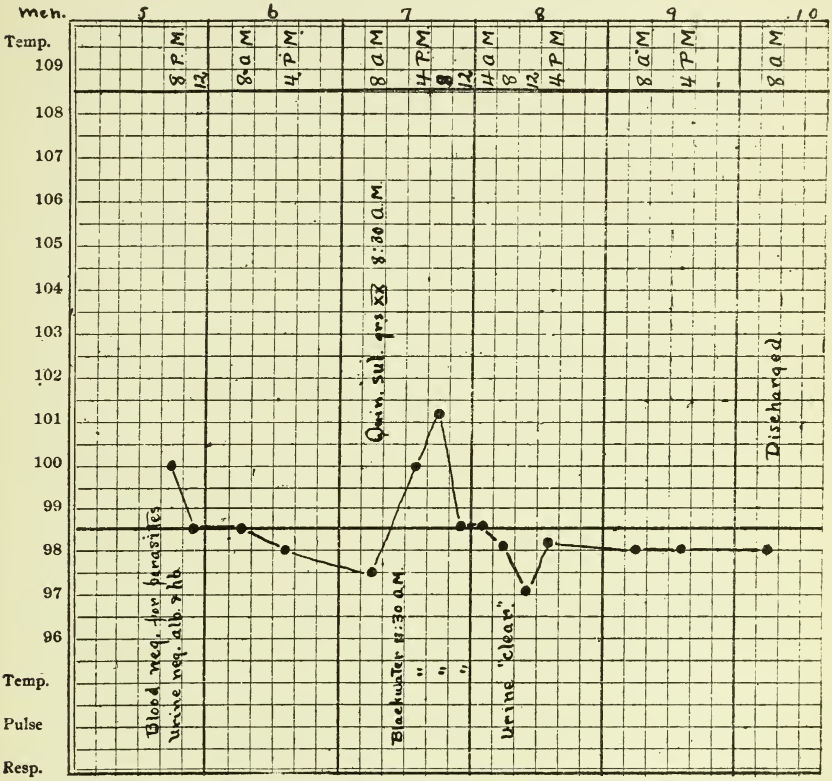

Chart 3.—No. 10,077. Patient, colored man from Antigua, W. I., who had been on the Isthmus five months, was admitted to Colon hospital, March 5, 1908. The patient passed "bloody urine" after taking quinin three weeks before admission. On the day before admission he felt sick and took 15 or 20 grains of quinin, after which he passed "bloody urine" again. After admission the urine was negative for albumin and hemoglobin. Quinin was withheld until the third day at 8:30 a. m., when 20 grains was given. "Blackwater" appeared at the third urination, two hours after quinin, and hemoglobinuria persisted until the next morning.

The differentiation of pernicious malarial fever with hemoglobinuria from erythrolytic hemoglobinuria rests chiefly on blood examinations. But occasionally parasites may not be numerous in the peripheral blood while they may be swarming in the internal organs. In such a case, cerebral symptoms (delirium, stupor or coma), which are rare in erythrolytic hemoglobinuria, may lead one to a correct diagnosis. The importance of the differentiation from the standpoint of treatment is obvious, for whatever may be one's belief regarding the treatment of erythrolytic hemoglobinuria, there can be no question but that in the pernicious malarial type the infection overshadows the hemoglobinuric condition, and that quinin in large doses must be introduced promptly into the blood-stream. If the patient is not vomiting and the attack seems only moderately severe, 10 grains of quinin in solution by mouth every three or four hours may be sufficient, the absorption being determined by tests for the drug in the urine. If vomiting supervenes, quinin must be

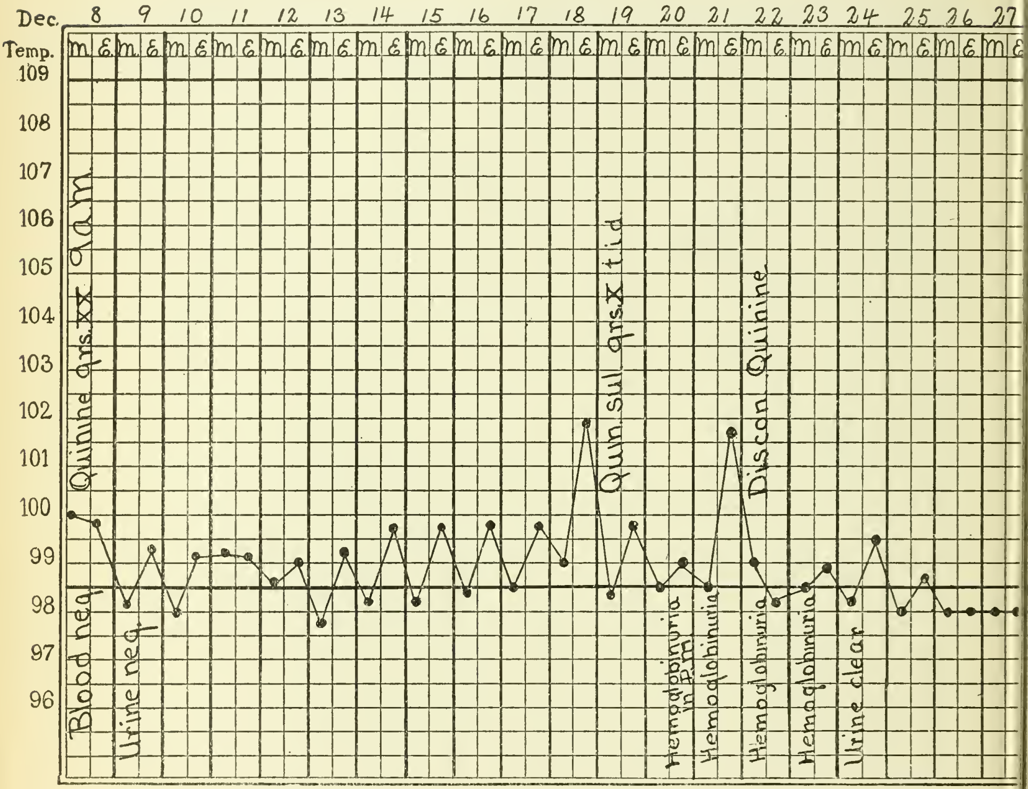

Chart 4.—No. 8,711. Patient, colored man from Jamaica, who had been in Panama two and a half years, was admitted to Colon hospital, Dec. 8, 1907. The patient had chill with blackwater Nov. 19, 1907, about nineteen days before admission. Hemoglobinuria did not follow one dose of quinin given on admission. After ten days quinin grs. x, t. i. d. was ordered, and hemoglobinuria developed the next day; it subsided when quinin was discontinued. The patient's brother was in the hospital at the same time with hemoglobinuria (Chart 15).

given by intramuscular injection or intravenously. In the severer infections an intravenous injection of 15 or 20 grains should be given at once and repeated every eight hours, for four doses. Between these doses 15 or 20 grains should be given by mouth or, if necessary, by intramuscular injections. It should be one's object to destroy the parasites

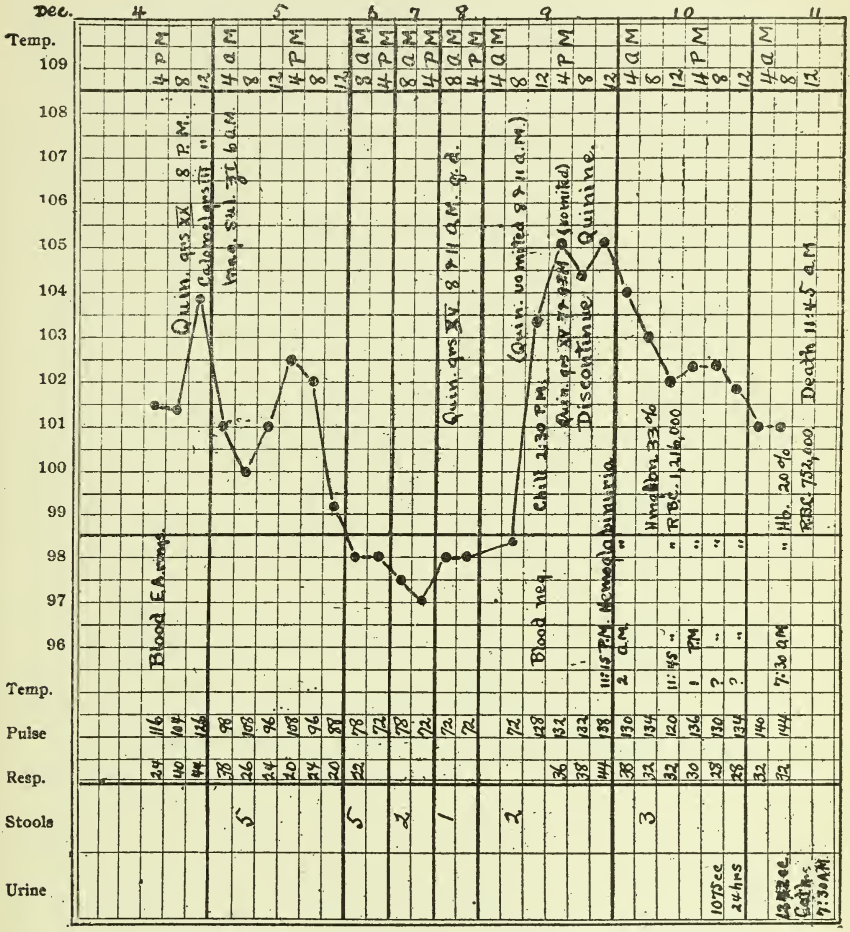

Chart 5.—No. 16,520. Patient, white, American, aged 21, from Fort Dodge, Iowa, who had been on the Isthmus four months, was admitted to Colon hospital, Dec. 4, 1908. The patient had had no previous malaria, had been sick three days and had taken quinin before admission. Quinin was ordered and 20 grains given on admission, but omitted by mistake afterward. The temperature dropped to normal and patient improved rapidly. On the third day of normal temperature the omission of quinin was discovered and it was re-ordered. On the following day a violent chill occurred, the temperature rose to 105, and hemoglobinuria followed. Quinin was discontinued, but the course was rapidly downward, urination was free, but blood destruction was extreme, and death took place forty-eight hours after the temperature began to rise.

in the intracorpuscular stage of the cycle, and thus to prevent them from reaching maturity. It seems certain that a large proportion of them can be killed in this stage, and the evidence is good that many infected corpuscles can be saved. (Case 1, hemoglobin and r. b. c. records).

ERYTHROLYTIC HEMOGLOBINURIA

This type of hemoglobinuria is of course the common one and the one under special discussion in this paper. The material for my study has been collected from the records of Ancon Hospital from 1904 to

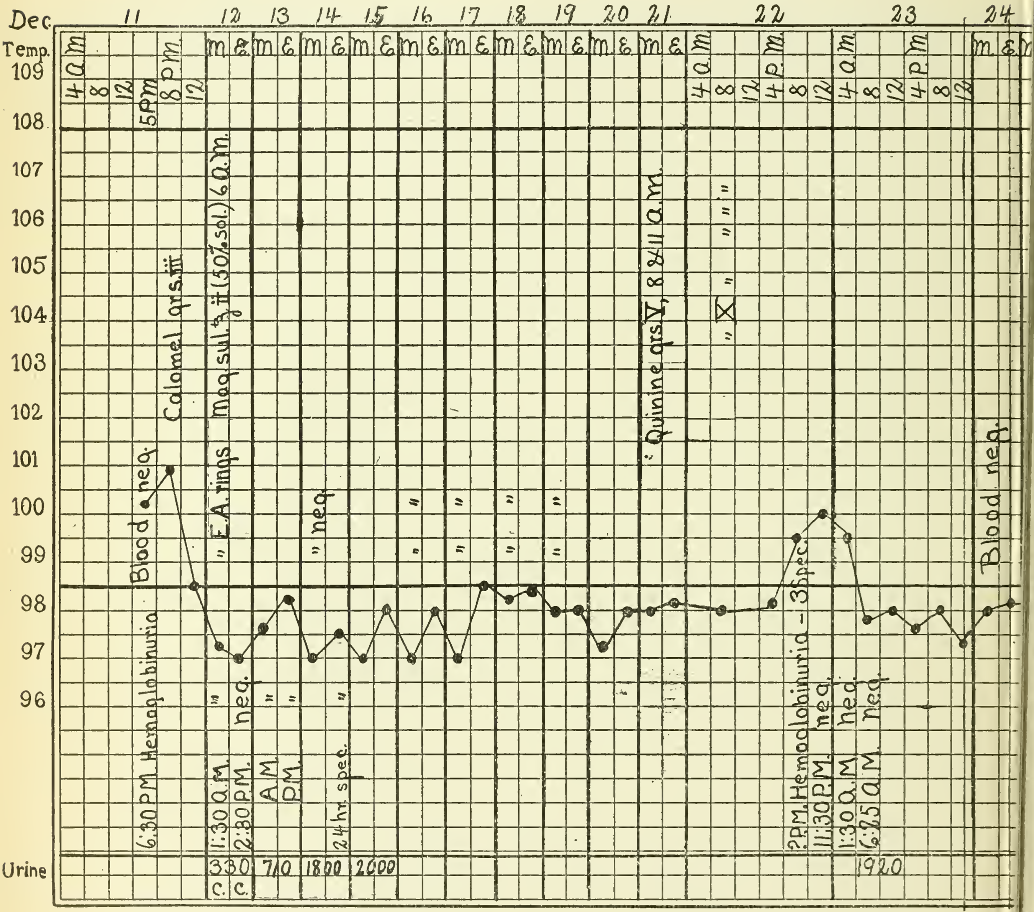

Chart 6.—No. 16,605. Patient, white, Austrian, who had been on the Isthmus one year, was admitted to Colon hospital, Dec. 11, 1908. The patient had had three previous attacks of "blackwater," had been sick two days, and had taken a quinin tablet every day for past ten days. On the morning of Dec. 11 the patient took 15 grains of quinin and at 4 p. m. noticed "blackwater." There was hemoglobinuria on admission. Estivo-autumnal (E. A.) parasites were found on second day. Quinin, grains x, were given on December 21 and grains xx on December 22. A transient hemoglobinuria followed.

April, 1910, 162 cases, and Colon Hospital from November, 1907, to May, 1910, fifty-nine cases—a total of 221 cases. For certain reasons all of the records of Colon Hospital prior to November, 1907, and many of the records of Ancon Hospital were not accepted and the cases excluded. There were eighteen recurrences in the hospitals among the 221 cases, and these have been considered separate attacks, since it sometimes happened that an initial attack was treated by one method while the recurrence was treated by another. The recurrences were considered separate attacks only when a period of not less than two days of hemoglobin-free urine intervened between attacks. There were, then, 239 attacks of blackwater represented by the 221 cases. These 221 cases include twenty cases previously reported by Gorgas,[4] which in turn included fourteen cases reported by me.[2] They include, also, Herrick's nine cases referred to in my report.[5]

The 221 cases have been divided into two series, the first of which includes cases directly or indirectly under my care, the second all other cases.

Series 1.—My cases, seventy-three patients, eighty-four attacks. (Hemoglobinuria verified in almost every attack by the demonstration of hemin crystals or by the guaiac and turpentine test.)

Series 2.—Other cases, 148 patients, 155 attacks. (Hemoglobinuria often verified by above tests and diagnosis often made from appearance of urine with a heavy transient albuminuria.)

GENERAL TREATMENT

The most important general measure is the introduction of fluids by mouth, by rectum, subcutaneously or intravenously. The passage of a large quantity of urine is of the utmost importance, for the gravity of the prognosis increases with a decreased urinary output, and the majority of patients who die have suppression of urine. Sweat baths and the various diuretics may be tried, but I think that little is to be expected from them, and there is always a possibility of drug irritation of the affected kidneys. In a large number of the cases of Series 2, however, Basham's mixture was used as a routine procedure, and there appears to have been no injury done by it, although no good either. The bowels should be opened with calomel (3 to 5 grains is sufficient) followed by a saline cathartic; or, if vomiting prevents, enemas may be used.

The diet should consist of nourishing liquids, and during convalescence the patient's appetite may be the guide.

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[4] Gorgas, W. C.: Malaria in the Tropics, Jour. Am. Med. Assn., 1906, xlvi, 1417.

[5] In order that no confusion may arise in future leading to repeated reports for mortality statistics of the same cases, a list of the hospital numbers of the cases included in this report is appended.

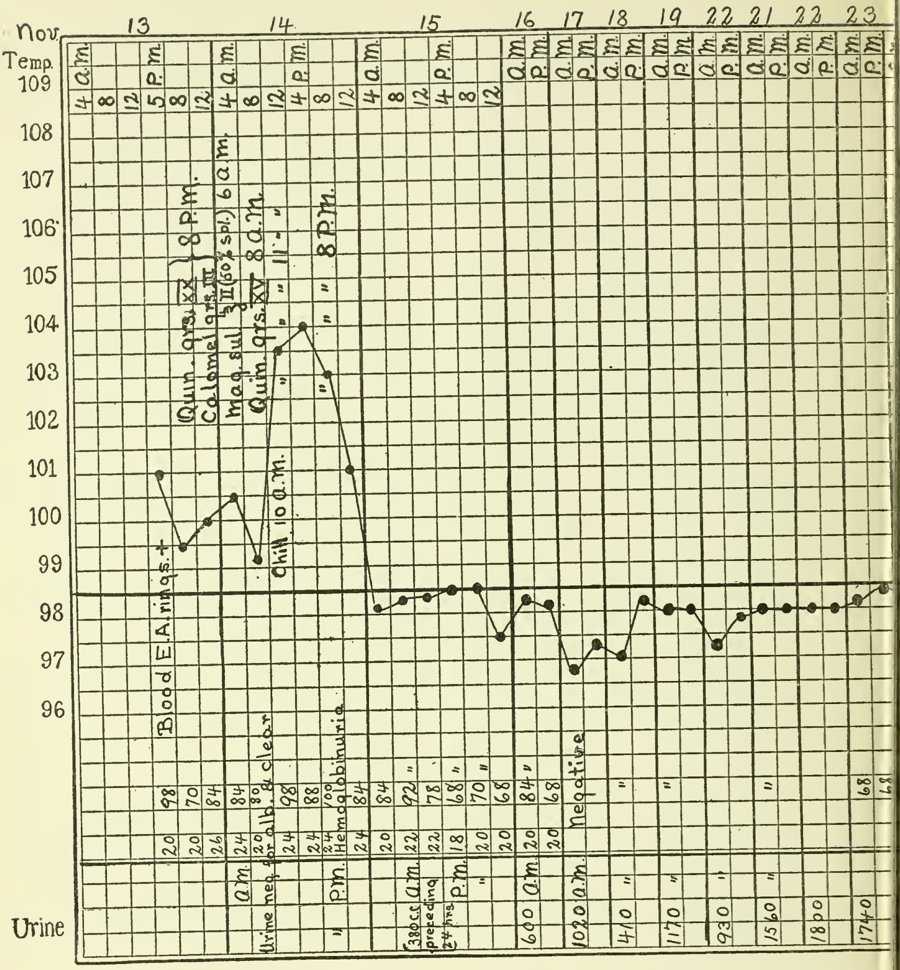

Chart 7.—No. 16,141. Patient, white, Spaniard, who had been in Panama nineteen months, was admitted to Colon Hospital July 25, 1909. The patient had had six previous attacks of malaria, and had been sick one day with present illness. Both attacks of hemoglobinuria in the hospital were apparently precipitated by quinin. Estivo-autumnal parasites were found on six separate examinations. Quinin was discontinued when hemoglobinuria developed, but when death approached quinin was ordered to be given by intramuscular injection. Autopsy was made fifteen hours after death. No parasites were found in smears from the brain, spleen, bone-marrow and liver.

For vomiting and restlessness morphin in repeated small doses given hypodermically is harmless and by far the most useful and satisfactory remedy. Crushed ice, also, may be useful.

Strychnin is the most satisfactory stimulant in cardiac or respiratory depression.

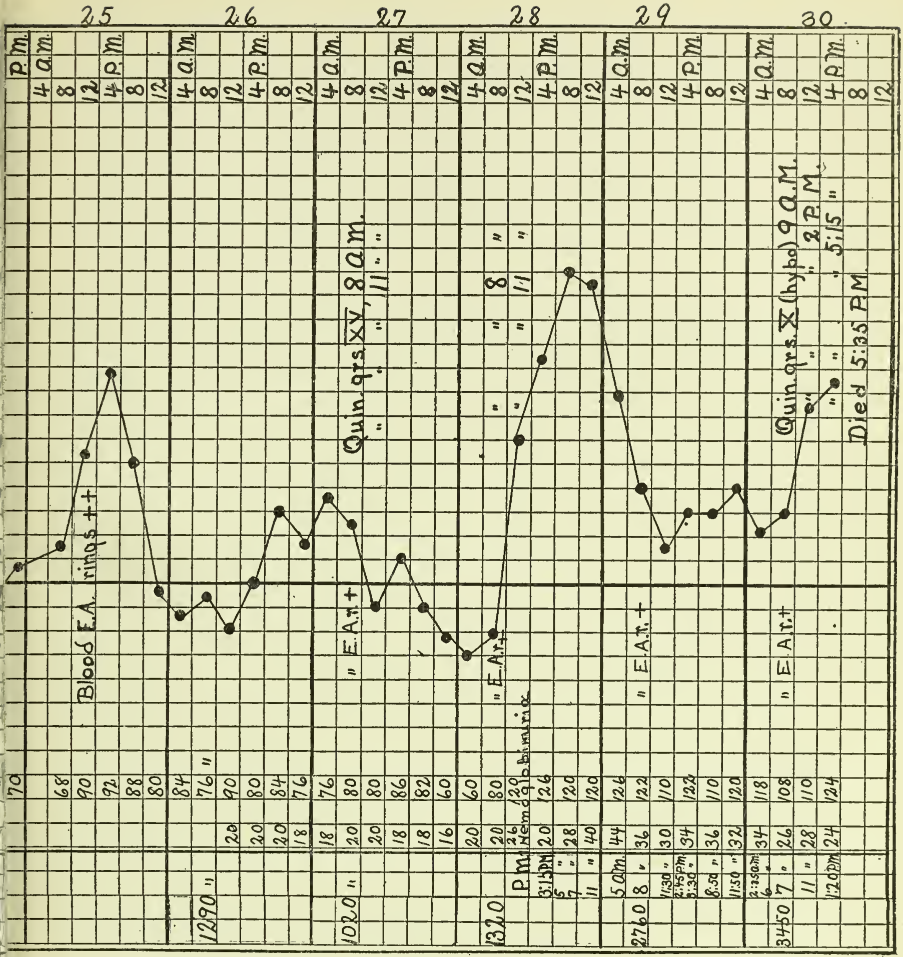

Chart 7—Continued

These general measures need little discussion, as they are ones on which all are practically agreed. I take it that the great question is still the one to be considered next.

QUININ TREATMENT

Relation of Quinin to Etiology.

Before one discusses whether or not it is wise to use quinin in the treatment of erythrolytic hemoglobinuria, it is meet that one's confession of faith be made regarding the relation that quinin bears to the onset of the disease. In Charts 2 to 11 inclusive, evidence that seems to be conclusive is presented in favor of the view that in certain cases, whatever may be the predisposing condition, quinin is the exciting cause. On the other hand, the recurrences in Charts 11, 12 and 13 furnish evidence that in other cases the onset may be in no way connected with the drug. The negative quinin history in the case represented by Chart 14 seems to be reliable. I have previously reported another attack occurring in an intelligent American who denied having taken quinin before the passage of blackwater.[2] The onset of many other attacks in this series was apparently associated with quinin (Chart 16), and in many the history was indefinite or not solicited. The charts referred to represent the attacks most strikingly illustrating the truth in the views that quinin is and is not the exciting cause. That the number of striking instances of attacks precipitated by quinin is greater than the number arising without it is due, partly at least, to the fact that evidence in favor of the latter

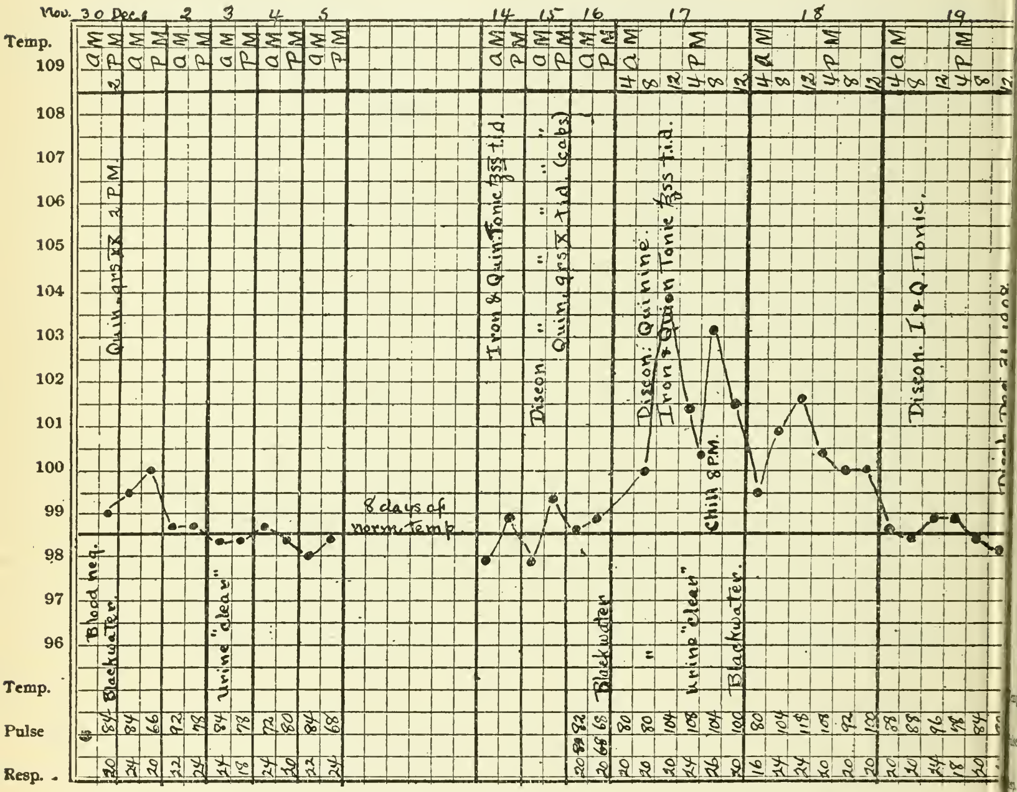

Chart 8.—No. 50,017. Patient, white, Spaniard, who had been on the Isthmus four and one-half months, was admitted to Ancon Hospital Nov. 30, 1908. The patient had been sick and passing "blackwater" five days before admission; had been jaundiced four days. "Blackwater" was present on admission. Recurrence followed iron and quinin tonic, which contained 15 grains of quinin in one ounce.

view is more difficult to obtain. More or less fever usually precedes the onset of blackwater, and residents practically always take quinin on the slightest suggestion of fever. It follows, then, that nearly all patients who have hemoglobinuria in Panama have taken quinin before the onset, but it would be absurd to conclude that quinin precipitated the condition in every case or even in the majority of cases.

To sum up, I am sure that a few attacks of erythrolytic hemoglobinuria are precipitated by quinin, and also that a few develop without

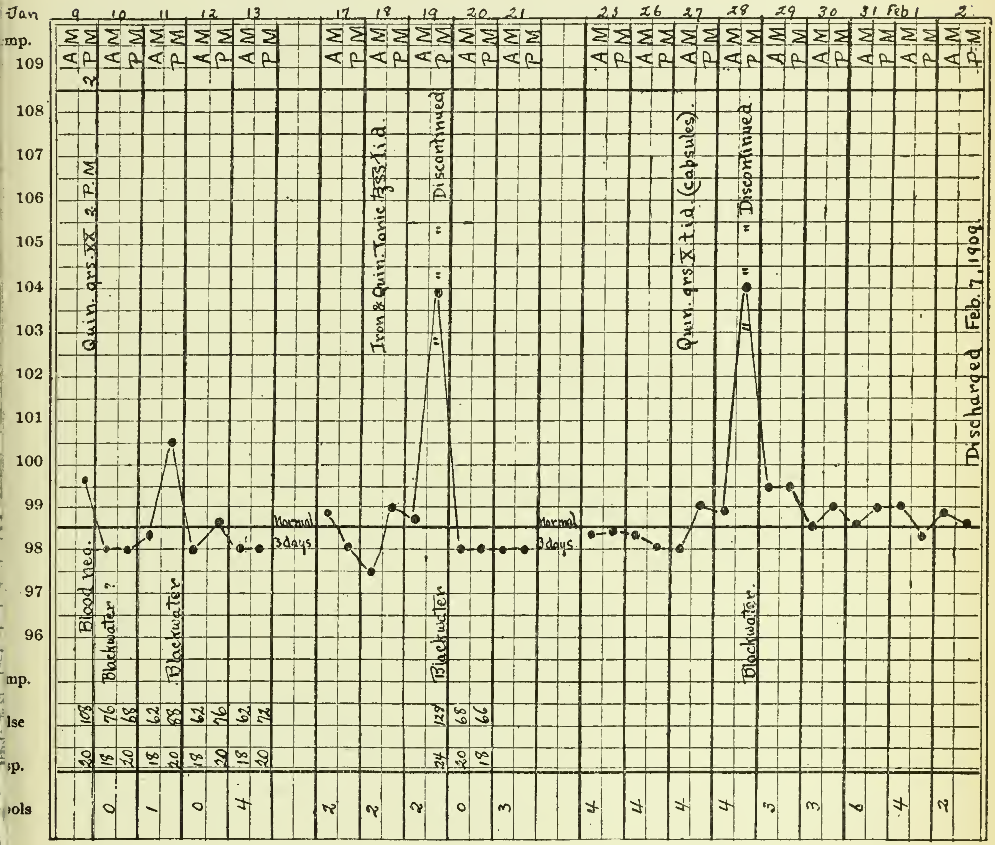

Chart 9.—No. 52,291. Patient, white, Jamaican, who had been on the Isthmus two years, was admitted to Ancon Hospital, Jan. 9, 1909. The patient had had "blackwater" on one previous admission to hospital. He had been sick three days and passed "blackwater" on day before second admission. Presence or absence of "blackwater" on admission was not stated in record. Iron and quinin tonic, 15 grains quinin to one ounce was given, and "blackwater" followed.

quinin, and good evidence is afforded that such is the case. I believe that a considerable number of the attacks that remain are precipitated by quinin and that a larger number are not connected with the drug, but I cannot present evidence in proof.

Our knowledge, so far, of the part that quinin plays in the etiology of erythrolytic hemoglobinuria does not aid us greatly, therefore, in settling the question of its use in the treatment. Attacks that are precipitated by quinin (such as those represented by Charts 2 to 11) of course should not be treated with quinin. But these attacks cannot be definitely separated from others except in occasional recurrences that take place while the patient is under observation and which follow promptly the administration of quinin after a period of apyrexia and hemoglobin-free urine.

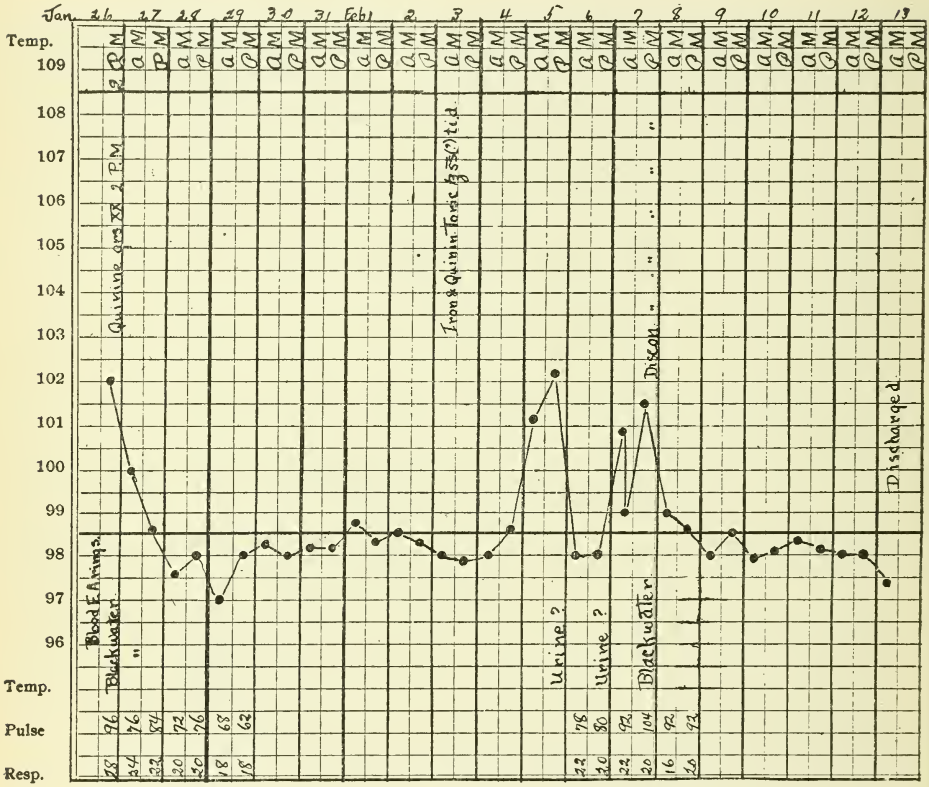

Chart 10.—No. 53,409 (Ancon). Patient, white, Italian, who had been on the Isthmus twenty-four months, was admitted to Ancon Hospital, Jan. 26, 1909. The patient had been previously admitted to hospital because of "blackwater"; had left hospital only nine days before second admission. He had been sick five days. The night before admission he passed "blackwater." Character of urine February 5 and 6 was not recorded, and the dose of iron and quinin tonic was not stated in record, probably half an ounce three times a day or quinin 7½ grains t. i. d.

One must turn to statistical studies and his own personal observations for guidance in a matter about which there is so much genuine difference of opinion.

Statistical Study

Deaderick's compilation of statistics in his recent book[6] practically settles the matter in favor of treatment without quinin. The summary is as follows:

	Cases.	Deaths.	Mortality.
Treated with quinin................	1821	472	25.9 %
Treated without quinin..............	1006	112	11.1 %
Treatment mixed or not recorded.....	3210	684	21.3 %

Deaderick thinks that "this number of cases probably eliminates all errors and should be convincing," in which opinion he is probably correct. My own statistics tend to confirm the above compilation, but the result is not nearly so striking. The difference may be partly a matter of interpretation, for I have found it not always an easy matter to classify a given case, and I have separated no class as having received mixed treatment, for the following reason. During the latter part of 1907 and the first eight months of 1908 we were treating all cases of blackwater fever with quinin in large quantities, usually by intramuscular injections. The treatment was never curtailed in severe cases, and all of the attacks could be placed frankly among those treated with quinin. In September, 1908, we began to treat a series of cases without quinin, and a certain number of them were of course severe and proceeded towards a fatal termination. It sometimes happened that the ward physician in immediate charge of such a case felt that nothing was being done for the patient, and the natural desire was that an attempt be made to do something, the courage required to watch the battle without interference failed, and the patient received quinin (Chart 7). It would certainly be misleading to take these fatal cases out of the class treated without quinin, for the mortality of this class would thereby be artificially lowered. I cannot but believe that this has happened to some extent in the statistics that Deaderick has done such able work in collecting. As for the mortality of the class treated with quinin, it is certain that in it have been placed all those cases of pernicious malaria in which hemoglobinuria was recognizable as "blackwater," and that these cases, belonging to the severest type of the disease, have very much increased the mortality of the class. After all is said, however, the difference is so great that one would be, perhaps, ultracritical not to accept the general indication of the statistics in favor of withholding quinin in erythrolytic hemoglobinuria.

An attempt has been made in analyzing the cases of this report to avoid errors like those indicated above, and the cases have been placed in the class to which they belonged when the course was downward and the prognosis became grave. This was sometimes a difficult question to decide, but in the main I think that the result is trustworthy.

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[6] Deaderick: Practical Study of Malaria, W. B. Saunders Co., Philadelphia, 1909, p. 299.

TABLE 1.—RESULT OF TREATMENT WITH AND WITHOUT QUININ

SERIES I: WRITER'S CASES, SEVENTY-THREE PATIENTS, EIGHTY-FOUR ATTACKS

Treated with quinin—	Attacks.	Deaths.	Mortality.
Whites	31	4	12.9 %
Blacks	10	4	40. %
Total	41	8	19.5 %
Treated without quinin—			
Whites	28	5	17.8 %
Blacks	15	2	13.3 %
Total	43	7	16.3 %

SERIES II: OTHER CASES, ONE HUNDRED FORTY-EIGHT PATIENTS, ONE HUNDRED FIFTY-FIVE ATTACKS

Treated with quinin—	Attacks.	Deaths.	Mortality.
Whites	36	5	13.9 %
Blacks	18	5	27.8 %
Total	54	10	18.5 %
Treated without quinin—			
Whites	83	12	14.5 %
Blacks	18	3	16.6 %
Total	101	15	14.8 %

SERIES I AND II: TWO HUNDRED TWENTY-ONE PATIENTS, TWO HUNDRED THIRTY-NINE ATTACKS

Treated with quinin—	Attacks.	Deaths.	Mortality.
Whites	67	9	13.4 %
Blacks	28	9	32.1 %
Total	95	18	18.9 %
Treated without quinin—			
Whites	111	17	15.3 %
Blacks	33	5	15.2 %
Total	144	22	15.3 %

The mortality of the white patients of each series and of the combined series shows a difference, under the two methods of treatment, so small that one death credited to the group of quinin-treated cases would even up the percentages. This difference is within the limits of error in classification. The mortality of colored patients treated without quinin is almost exactly equal to that of white[7] patients, while of those treated with quinin more than double the percentage died. As far as the statistics go, therefore, they appear to indicate that in regard to life it makes little difference whether or not white patients receive quinin, while from colored patients it should be withheld.

Personal Observations

In a former communication[2] I concluded that quinin was strongly indicated in "malarial hemoglobinuria," that it should be given in large doses, and that properly given it appeared to be almost a specific. I beg leave here to abandon that view, which I consider now to be erroneous. In spite of the fact that my mortality statistics present only qualified support of the antiquinin view, observation of a fair number of cases treated by both methods has convinced me that quinin does no good in any case of erythrolytic hemoglobinuria, and that in many it is emphatically injurious. With it the patients usually suffer more, the disease is more frequently severe, and in many instances the fever and the passage of blackwater are prolonged in a manner that one rarely sees when quinin is withheld (Chart 16). Weight is added to this view by the cases cited in which quinin certainly precipitated the attack, and by the less striking evidence that there are numbers of other instances in which the drug was probably responsible for the onset. In a number of cases, also, hemoglobinuria persisted while quinin was being given, but promptly ceased when it was withheld (Chart 15).

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[7] The kidneys of blacks appear to be much more susceptible to injurious influences than the kidneys of whites.

TABLE 2.—RESULT OF TREATMENT WITH AND WITHOUT QUININ IN BOTH THE PRESENCE AND ABSENCE OF MALARIAL PARASITES

	PARASITES PRESENT						PARASITES ABSENT					
	Quinin+			Quinin—			Quinin+			Quinin—		
	No. attacks.	No. deaths..	Mortality per cent..	No. attacks.	No. deaths..	Mortality per cent..	No. attacks.	No. deaths..	Mortality per cent..	No. attacks.	No. deaths..	Mortality per cent..
Whites (Series 1).....	7	1	14.3	15	3	20	24	3	12.5	13	2	15.4
Whites (Series 2).....	18	4	22.2	31	4	12.9	18	1	5.6	52	8	15.4
Total (Series 1 and 2)..	25	5	20.0	46	7	15.2	42	4	9.5	65	10	15.4
Blacks (Series 1).....	3	1	33.3	7	1	14.3	7	3	42.9	8	1	12.5
Blacks (Series 2).....	9	1	11.1	3	1	33.3	9	4	44.4	15	2	13.3
Total (Series 1 and 2)..	12	2	16.7	10	2	20.0	16	7	43.7	23	3	13.0
Whites and blacks (Series 1)...........	10	2	20.0	22	4	18.2	31	6	19.4	21	3	14.3
Whites and blacks (Series 2)...........	27	5	18.5	34	5	14.7	27	5	18.5	67	10	14.9
Total (Series 1 and 2)..	37	7	19.0	56	9	16.1	58	11	19.0	88	13	14.8

Relation of Malarial Parasites to Quinin Therapy

Writers on blackwater fever have usually divided the cases into two groups according to the presence or absence of malarial parasites in the peripheral blood, and have recommended that quinin be employed in treating the first group and withheld from the second. Deaderick[8] and Stephens[9] are exceptions to this rule. It is Deaderick's opinion that "the only conditions in which quinin is indicated are, first, where the parasites show no tendency to disappear after forty-eight hours from onset; second, in the infrequent cases of intermittent hemoglobinuria where the outbreak corresponds with parasitic sporulation." Stephens goes a little further and says, "if parasites still persist with a continuance of the fever then the question must be carefully weighed...If it can be avoided we should say it is better to abstain." Deaderick was unable to divide the cases of which he collected reports into groups according to the presence or absence of parasites. The attacks of the present report, however, can be grouped in such a manner and they bear on this point.

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[8] Deaderick: Practical Study of Malaria, p. 383.

[9] Stephens: Osler's Modern Medicine, i, 458.

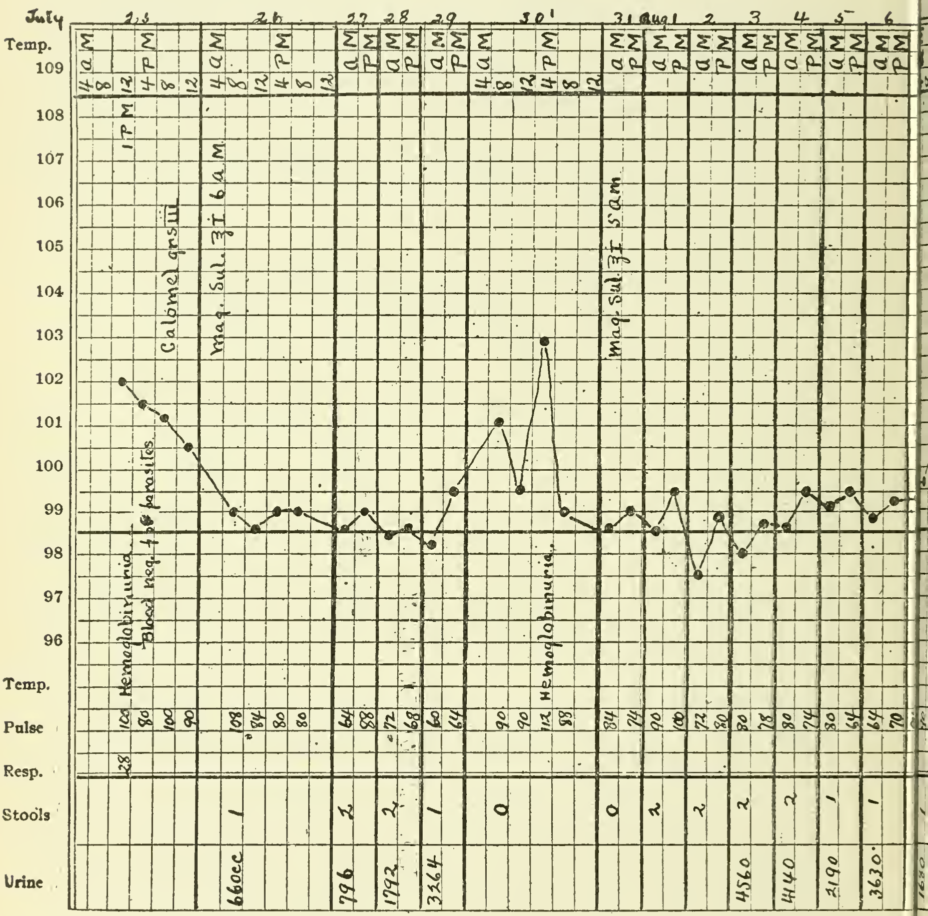

Chart 11.—No. 19,162. Patient, white, Spaniard, who had been on the Isthmus nineteen months, was admitted to Colon Hospital July 25, 1909. The patient had had malaria eight times previously, and before admission had been sick three days; had taken quinin and on the second day had passed "blackwater." He had been taking 9 grains of quinin daily before onset of the present illness. There were two recurrences; one arose spontaneously and one after taking quinin.

The whites of the "parasites present" group show a considerably higher mortality with quinin treatment than without it; the whites of the "parasites absent" group show a higher mortality without quinin than with it. The mortality among the blacks occurs somewhat more according to expectation. The mortality of the combined whites and blacks of both groups is slightly smaller in the attacks treated without quinin. Therefore the presence or absence of malarial parasites appears to make no difference in the mortality. Nor have I been able to detect any difference in the clinical courses of members of the two groups.

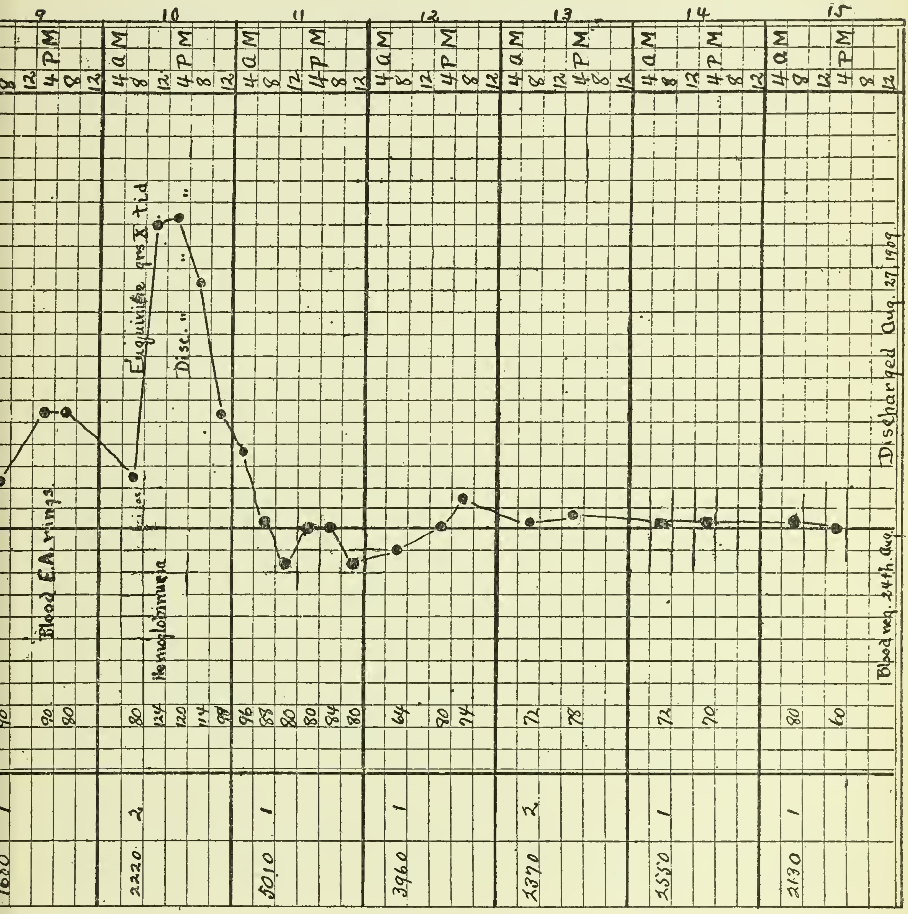

CHART 11—Continued

It is my opinion, therefore, that Deaderick and Stephens are quite right, as far as they go, in advising the withholding of quinin in most cases of blackwater fever, even if parasites be present in the blood. I should go a little further, however, and say that quinin should never be given during the passage of blackwater in cases belonging frankly to the erythrolytic type of hemoglobinuria. If parasites persist in or return to the peripheral blood during convalescence, as frequently happens, or if a malarial type of fever recurs, quinin may be given with caution, beginning with small doses and gradually increasing. It may be fatal to begin at once with large doses of quinin (See Chart 7).

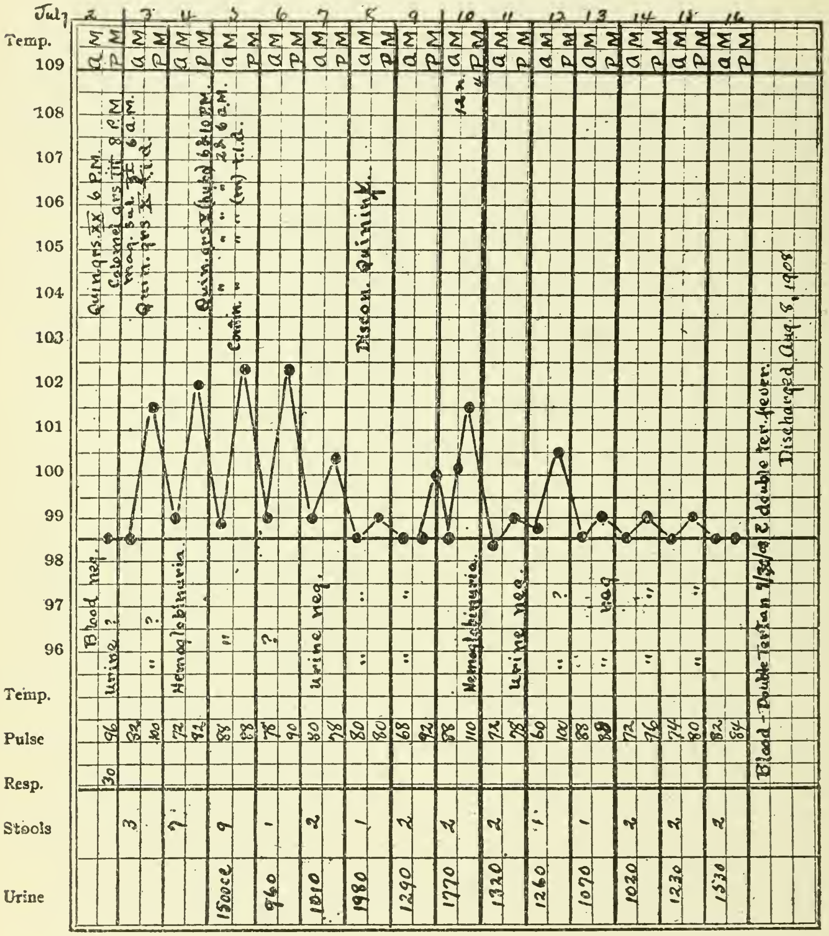

Chart 12.—No. 12,145. Patient, white, Spaniard, who had been on the Isthmus six months, was admitted to Colon Hospital July 2, 1908. The patient had had no previous malaria (?)—the present being the first time in hospital—and had never passed black urine. The patient had been sick four days and had taken quinin in solution twice daily since onset. The urine was "highly colored," but not black. It is not certain from the record whether or not the patient had "blackwater" on admission. It apparently developed on the third day in the hospital. There was a recurrence three or four days after hemoglobinuria had ceased and two days after quinin had been discontinued. The double tertian infection possibly occurred in the ward. Quinin was given, 10 grains, t. i. d., and "blackwater" did not develop.

Serum Therapy

It would scarcely be proper to close without referring to the work of Christophers and Bentley[10] and their suggestion that a serum therapy, such as that used in paroxysmal hemoglobinuria, is possibly in sight. Their work on iso-agglutinins and isohemolysins and their conclusions[11]

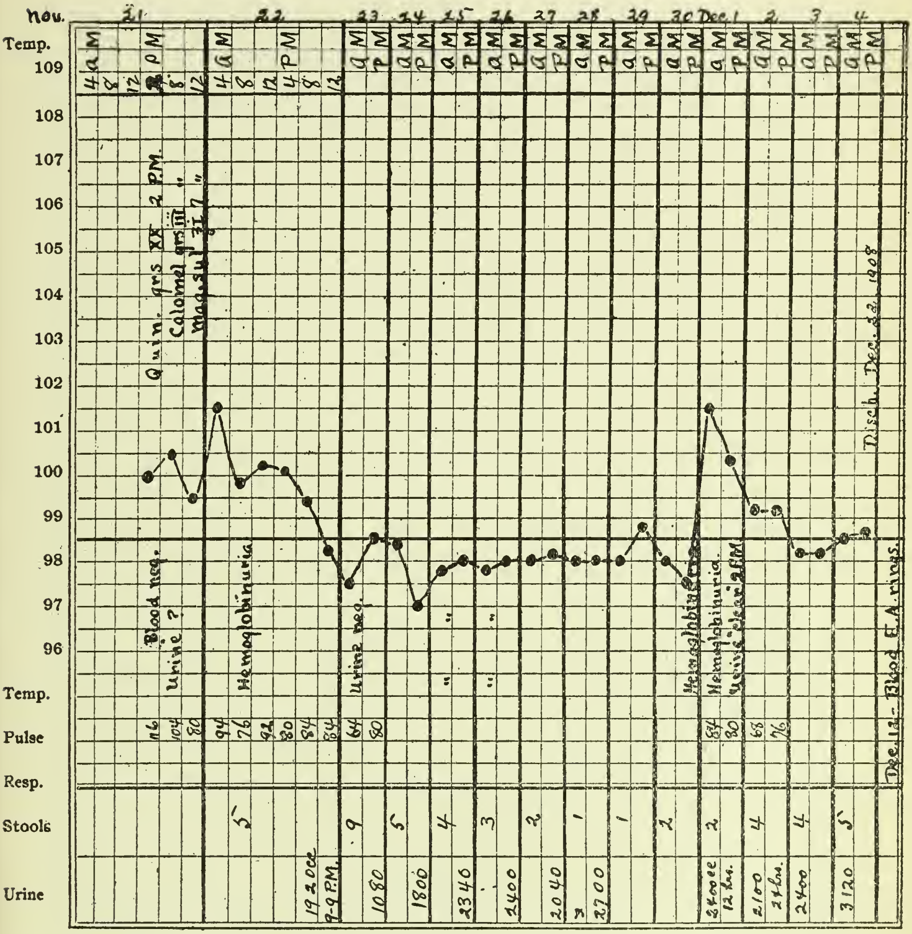

Chart 13.—No. 49,539. Patient, white, Portuguese, who had been on the Isthmus fifteen months and in hospital four times, was admitted to Ancon Hospital Nov. 21, 1908. The patient had been sick three days, passing "blackwater" two days. There was spontaneous recurrence of hemoglobinuria. Fever recurred on Dec. 12 and estivo-autumnal organisms were found. The patient was given 30 grains of quinin daily without recurrence of "blackwater."

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[10] Christophers and Bentley: Blackwater Fever, Scient. Mem. Gov. India. (new series), 1908, No. 35, pp. 181, 182.

[11] Christophers and Bentley: Blackwater Fever, Scient. Mem. Gov. India. (new series), 1908, No. 35, pp. 154-179.

are interesting, but in the light of Moss'[12] recent extensive and excellent studies of normal and pathologic bloods, it seems probable that they misinterpreted their results, attributing to the influence of malaria merely normal variations of serums and corpuscles. When their monograph came into my hands, I attempted to repeat some of their work,

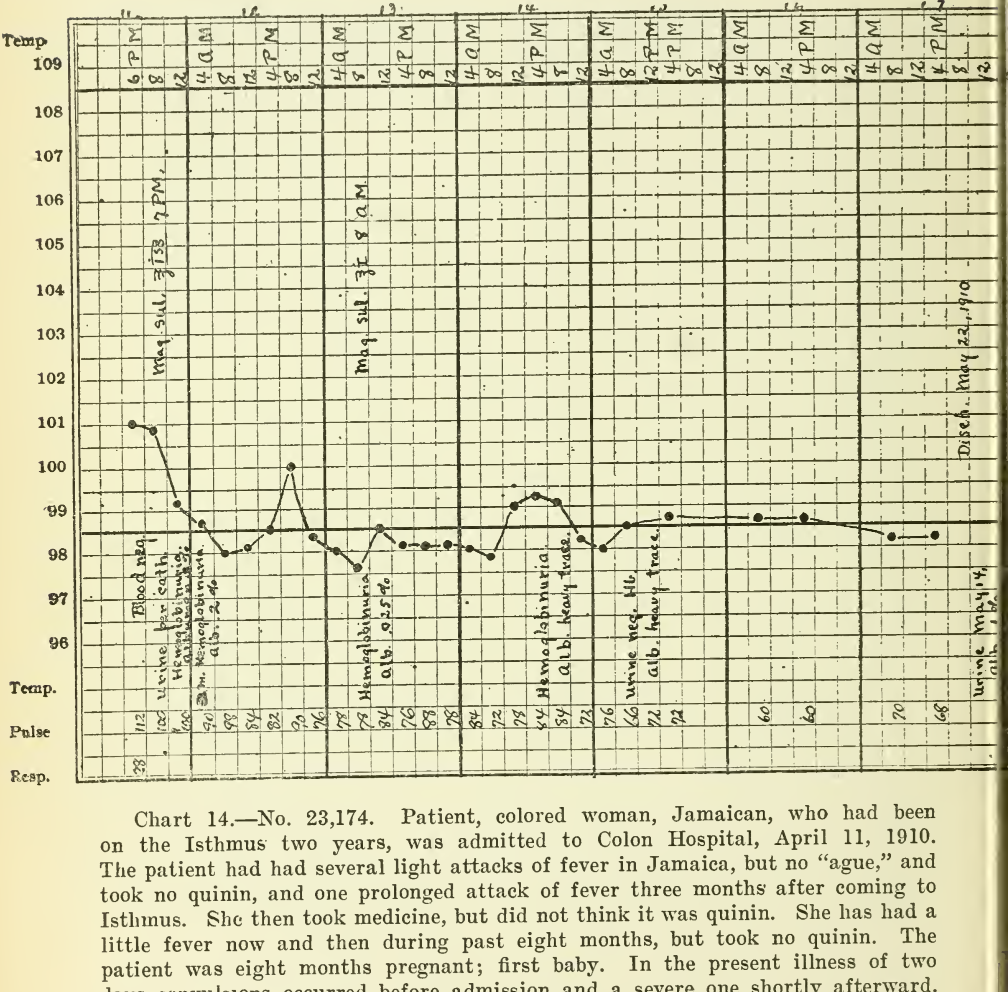

Chart 14.—No. 23,174. Patient, colored woman, Jamaican, who had been on the Isthmus two years, was admitted to Colon Hospital, April 11, 1910. The patient had had several light attacks of fever in Jamaica, but no "ague," and took no quinin, and one prolonged attack of fever three months after coming to Isthmus. She then took medicine, but did not think it was quinin. She has had a little fever now and then during past eight months, but took no quinin. The patient was eight months pregnant; first baby. In the present illness of two days convulsions occurred before admission and a severe one shortly afterward. The patient was semicomatose, passed very little urine. She had taken no quinin. There was no uterine hemorrhage. Urine per catheter showed hemoglobinuria, albumin 0.8 per cent. (Esbach). Recovery was good. Patient did not abort. On May 4 the patient developed toxemia and labor was induced under stovaine anesthesia. Good recovery and child lived. Urine on May 14 showed albumin 0.1 per cent., hyaline and hyalogranular casts.

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[12] Moss, M. L.: Isoagglutinins and Isohemolysins, Bull. Johns Hopkins Hosp., 1910, xxi, 63.

but in the beginning I met results which were incapable of explanation by their hypotheses, and which were explained only when Moss' paper appeared. Moss was able to classify all human bloods into four groups according to the agglutinating reactions of serums and corpsucles. With this classification as a working basis, we shall be able now to approach the study of the blood in erythrolytic hemoglobinuria with a degree of comprehension hitherto not possessed.

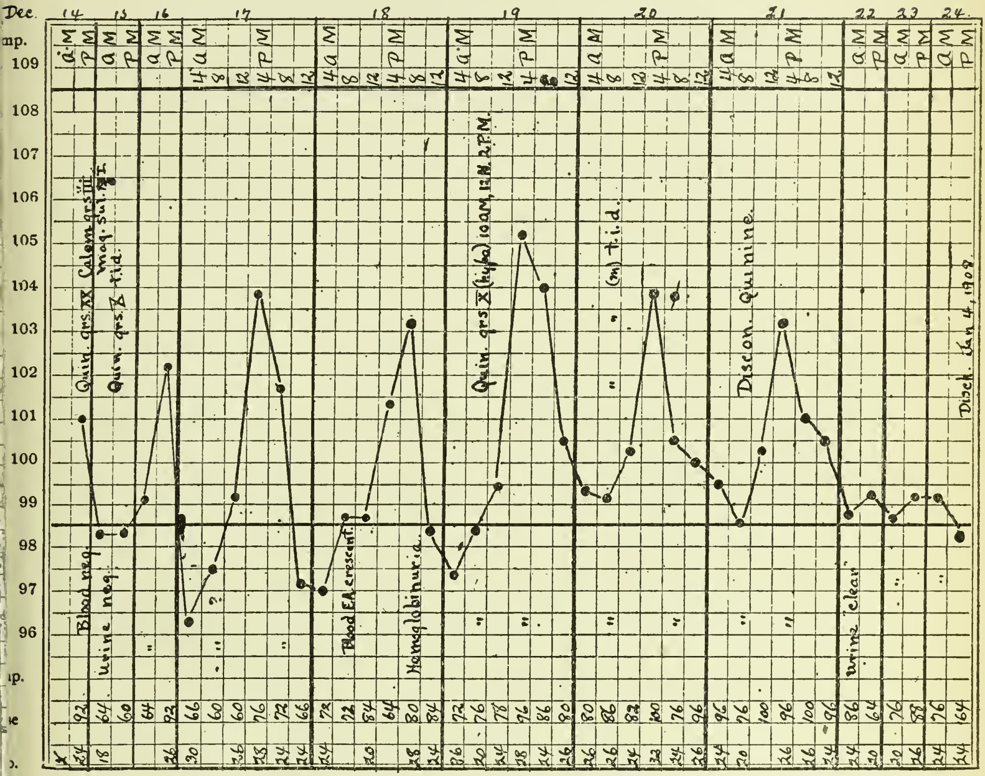


Chart 15.—No. 8,877. Patient, colored man, Jamaican, who had been on the Isthmus three years, was admitted to Colon Hospital Dec. 14, 1907. The patient had "blackwater" fever in Jamaica, 1903; no quinin had been given previous to onset; patient treated with quinin and "blackwater" lasted six days. "Blackwater" fever again occurred on the Isthmus, March, 1907, but the patient did not remember whether or not he took quinin before onset; he was then treated with quinin by intramuscular injection, and "blackwater" continued five days. On present admission no "blackwater," which was apparently precipitated by quinin and continued until quinin was discontinued. Patient's brother was in hospital at same time with "blackwater," apparently precipitated by quinin (Chart 4).

SUMMARY

1. Blackwater fever is a term that includes two types of hemoglobinuria more or less definitely associated with malaria. It is important

that the two types be separated for study and treatment. The indications for treatment are diametrically opposed. The two types probably differ in the mechanism of their production and their clinical phenomena are different.

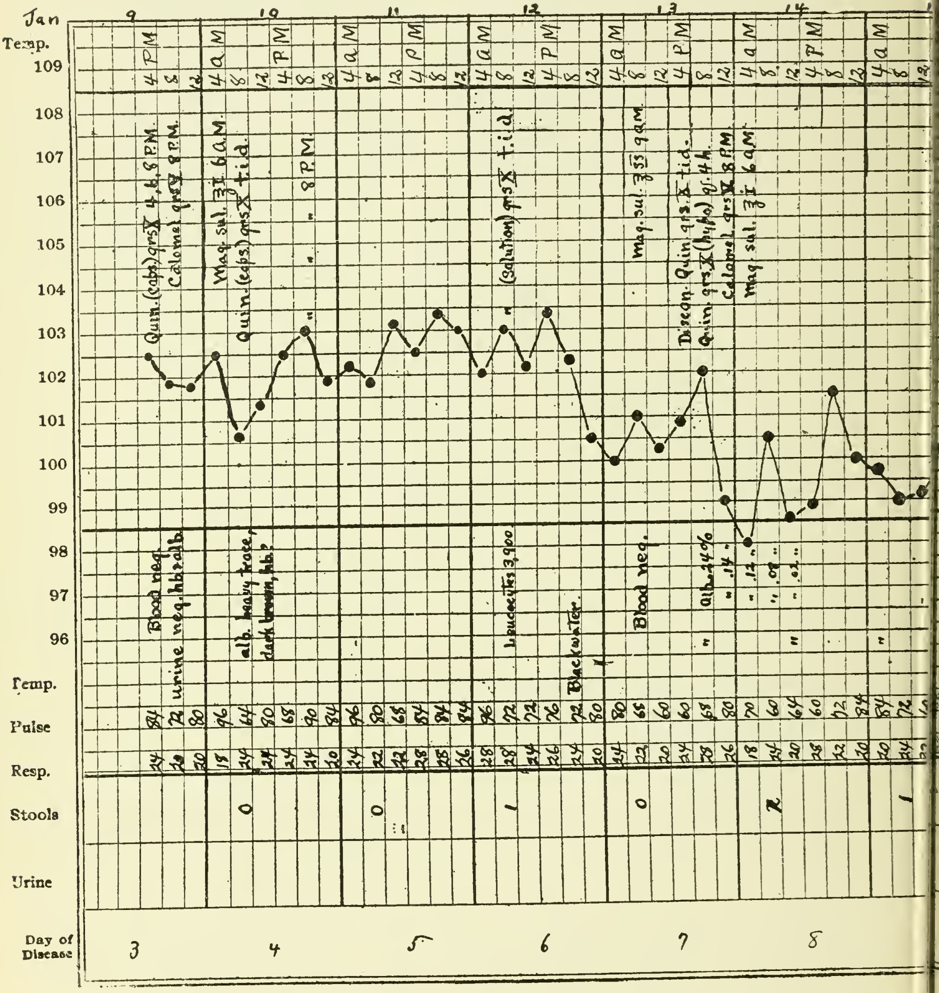
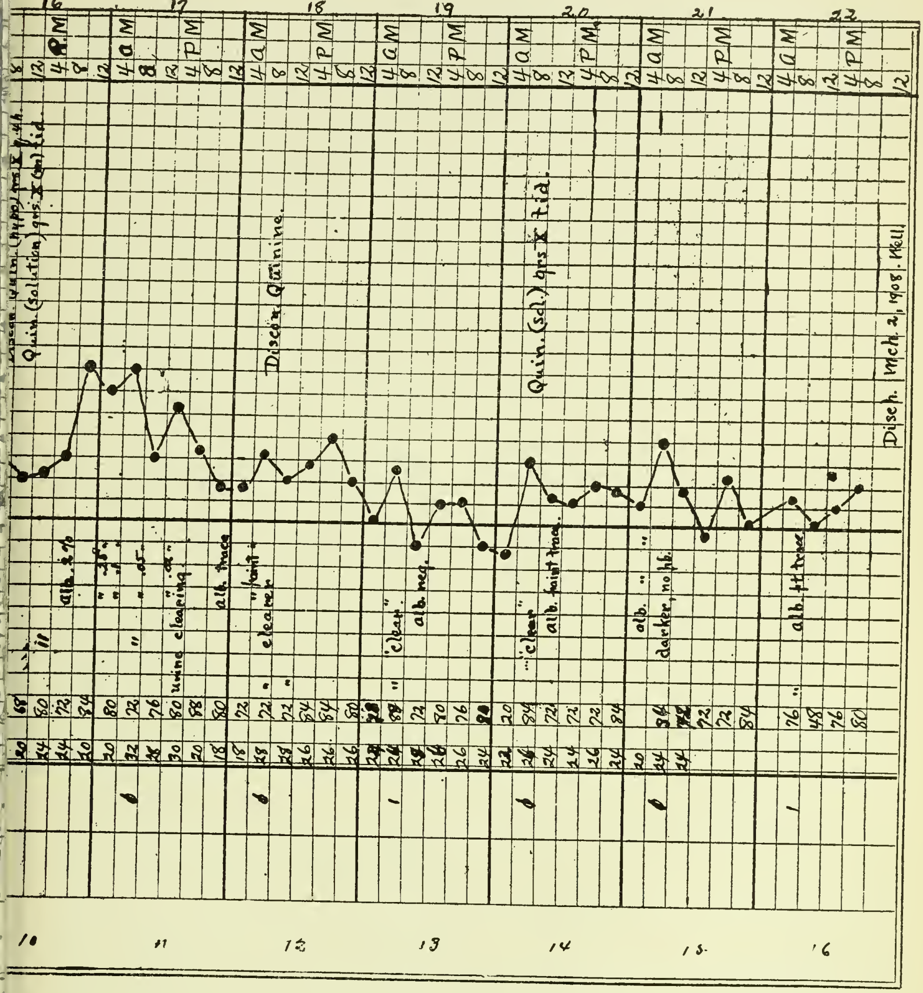


Chart 16.—No. 9,322. Patient, white, Australian, who had been on the Isthmus over three years, was admitted to Colon Hospital, Jan. 9, 1908. The patient had had fever three times previously. "Blackwater" fever occurred three years ago on the Isthmus. Onset occurred Jan. 7, 1908, with chill and fever; January 8, chill fever and "blackwater." Quinin history was not recorded. There was no "blackwater" on admission, but continued fever, possibly "post-hemoglobinuric." Quinin in solution was given on January 12 and hemoglobinuria developed that night. The patient was treated vigorously with quinin. Prolonged, severe course followed. The hemoglobin fell to 30 per cent. January 18. Widal test was negative January 18 and 22.

2. Type 1.—Hemoglobinuria associated with pernicious malarial infections. The hemoglobinuria is probably brought about by immediate destruction of erythrocytes by enormous numbers of sporulating parasites, and the time of its appearance can generally be foretold with a



fair degree of accuracy. The treatment is that of pernicious malarial fever. Type 2.—Hemoglobinuria indefinitely associated with malaria and probably brought about by the solution of erythrocytes by an unknown hemolysin.

3. It is proposed that the terms "blackwater fever," "malarial hemoglobinuria," "hemoglobinuric fever," etc., be abandoned and that the two types of hemoglobinuria hitherto embraced by them be known as follows:

Type 1.—Pernicious malarial fever with hemoglobinuria.
Type 2.—Erythrolytic hemoglobinuria.

4. A number of attacks of erythrolytic hemoglobinuria in this series of cases were precipitated by quinin, a large number of attacks were apparently precipitated by quinin, and a few recurrent attacks developed in the wards when no quinin had been given.

5. Statistical studies of 239 attacks of erythrolytic hemoglobinuria, supplemented by personal observation indicate that quinin should never be given during hemoglobinuria.

6. The presence of malarial parasites in the blood of patients with erythrolytic hemoglobinuria has no effect on the mortality or on the clinical phenomena, and affords no indication for treatment during hemoglobinuria. When parasites persist or reappear during convalescence or when fever persists or recurs after the cessation of hemoglobinuria, quinin should be given guardedly. The dose should be small at first and gradually increased, if hemoglobinuria is not precipitated.

REPORT OF CASES[13]

Case 1 (Chart 1).—Pernicious malarial fever with hemoglobinuria, No. 23,811.

Blood Examinations

Time.	Hemoglobin (Sahli hemom.).	R. B. C. per c.mm.	Color index	Number R. B. C. counted.	Number infected.	Percentage infected.
15— p. m.	..	....	..	500	78	15.6
16— 9:00 a. m.	..	....	..	500	47	9.4
16—10:00 a. m.	85	....	..	....	..	....
16—11:30 a. m.	..	....	..	500	27	5.4
16— 4:00 p. m.	..	....	..	500	23	4.6
16— 4:30 p. m.	85	4,760,000	.89	....	..	....
16— 7:00 p. m.	..	....	..	500	18	3.6
16—12:00 m.	..	....	..	500	9	1.8
17— 4:00 a. m.	..	....	..	3,500 (approx.) 20 fields*	16	.46
17— 8:30 a. m.	..	....	..	4,500 (approx.) 25 fields	6	.13
17— 9:30 a. m.	93	5,192,000	.9	....	..	....
17— 4:00 p. m.	..	....	..	5,000 (approx.) 25 fields	5	.1
18— 8:00 a. m.	93	4,872,000	.95	50 fields	0	0
18— 3:00 p. m.	..	....	..	50 fields	0	0
19—10:00 a. m.	..	....	..	50 fields	0	0
19— 4:00 p. m.	91	....	..	....	..	....
20— 1:30 p. m.	84	5,008,000†	.84	....	..	....
25—10:00 a. m.	81	....	..	....	..	....

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[13] Only Case 1 is discussed in detail. Synopses of the other cases (2-16) appear as legends under the respective charts.

* B. and L. objective 1/12 and ocular 1. Actual counts of the corpuscles in a number of fields in which the corpuscles were more and less thickly spread varied from 175 to 250 per field. The estimates were made from these standards, taking into consideration the thickness of the smear.

† 8:30 a. m.

				ing)	Negative	Mucous cloud	A few hyaline and hyalo-granular casts; no r. b. c.
16— 1:30 p. m.	Brownish-yellow	1,033	Acid	Faint trace	Negative	None	A few hyaline and hyalo-granular casts; no r. b. c.
16— 4:40 p. m.	Brownish-yellow	1,030	Acid	Trace	Suspicious	Pus Shred	A few hyaline and hyalo-granular casts; no r. b. c. + pus cells
17— 5:30 a. m.	Blackwater, dark, cloudy, smoky, brownish-red by transmitted light	1,028	Alk.	Will not settle in Esbach tube; 25 per cent. wet	Intense reaction	Heavy, grayish-brown	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c.
17—11:00 a. m.	Blackwater, yellowish-red, less intense	1,025	Acid	Heavy trace	Supernatant urine; 1-100 dil. is robin-blue; sediment is blue-black (1-100)	Heavy, greenish brown	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c.
17— 5:15 p. m.	Suggests black water, brownish-red, less intense	1,023	Acid	Heavy trace	Mixed urine; 1-10 dil. is violet-blue	Heavy, greenish brown (less)	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c. (fewer casts)
17—10:40 p. m.	Yellowish-red, not like blackwater	....	....	Trace	Supernatant urine; 1-10 is violet-blue	Mucous cloud	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c. (few casts)
18— 4:45 a. m.	Yellowish-red, not like blackwater	....	....	Trace	Undiluted urine is violet-blue	Mucous cloud	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c. (few casts)
18—10:20 a. m.	Yellowish-red, not like blackwater	....	Acid	Faint trace	Undiluted urine is violet-blue	Mucous cloud	Brown amorphous detritus; numerous hyalo-granular casts, covered with brown material; no r. b. c. (few casts)
18— 4:30 p. m.	Yellowish-red, not like blackwater	....	Acid	Very faint	Supernatant urine is negative; sediment is violet-blue	Very slight	Very few hyaline and hyalo-granular casts; no r. b. c.
19— 3:10 a. m.	....	1,023	....	Very faint	Supernatant urine is negative; sediment is violet-blue	Very slight	
19—10:20 a. m.	....	1,022	...	Negative	Negative	Very slight	
19— 3:00 p. m.	....	....	....	Negative	Negative		
20— 8:00 a. m.	....	....	....	Negative	Negative		

Patient.—Colored man, Martiniquan, aged 30, laborer, admitted May 15, 1910, 4 p. m.

History.—The patient had been on the Isthmus thirty-one months, had had seven previous attacks of fever in Panama, and many in Martinique. During fever attacks he had never noticed that urine was black or red. He said that he had been sick three days with fever, vomiting and headache, and had not taken quinin before admission.

Examination.—The patient was very restless on admission, tossing from side to side in bed and complaining of great pain in his head. His mind seemed fairly clear. Examination of heart, lungs and abdomen was negative; the spleen was not palpable. The blood was found to contain enormous numbers of small ring forms of estivo-autumnal malarial parasites. The imminence of hemoglobinuria was suspected and every specimen of urine was ordered to be sent when voided to the laboratory.

Course of Illness.—On the following day, May 16, the patient was quiet, but seemed very ill and extremely prostrated. Leukocytes numbered 7,100. At 8 p. m. his temperature rose abruptly from normal to 102 F. There was no chill, but vomiting occurred. The next urine voided, at 5:30 a. m. May 17, had the characteristic appearance of "blackwater." The patient did not pass into coma, or even lose consciousness, but he appeared to be extremely ill and profoundly depressed. The sclerotics became slightly jaundicd, but the spleen never became palpable or enlarged to percussion. Hemoglobin could be detected in the urine in traces until 3:10 a. m., May 19. Improvement was rapid from May 18 onward.

DISCUSSION OF THE CASE

Blackwater was prognosticated from an examination of the blood. More than 15 per cent. of the red corpuscles in the peripheral blood were infected. The number infected in the internal organs was probably much larger. In spite of the enormous infection, hemoglobin estimations and erythrocyte counts indicated but slight blood destruction, and the results were in striking contrast to the blood-picture in erythrolytic hemoglobinuria, in which, even in mild cases, blood destruction, as indicated by the same methods, is terrific. (Other cases have confirmed the blood findings given above.) The increase of hemoglobin and erythrocytes on May 17 was probably due to concentration of blood from loss of fluid by vomiting and urination. It seems quite certain that quinin in this case not only killed parasites in the intracorpuscular stage, but also prevented the destruction of many infected corpsucles. The parasites themselves showed evidence of the influence of quinin by their vacuolated and often bizarre appearance. The urine did not differ from the ordinary "blackwater" urine.

In conclusion, I wish to thank Colonel Gorgas for permitting me the use of the above material, and for consenting to the publication of the paper.

HOSPITAL NUMBERS OF CASES INCLUDED IN ABOVE REPORT

ANCON HOSPITAL CASES, 162

98
400
535
542
1,401
1,469
2,065
2,721
3,060
4,263
4,266
4,515
6,418
6,970
7,110
8,408
8,823
9,004
9,372
9,925
10,107
10,163
10,474
11,627
11,991
12,271
12,383
12,506
653
13,445
459
463
879
14,369
15,093
938
945
16,525
979
17,018
18,109
363
489
981
19,329
20,304
158
222
231
433
21,975
22,428
762
23,320
23,573
719
831
25,282
304
362
575
26,308
31,457
32,205
34,115
125
.....
36,162
249
534
38,349
711
735
47,423
525
605
637
781
788
48,075
384
49,146
303
317
419
446
539
50,017
980
51,364
607
753
758
969
971
52,192
206
291
386
454
479
496
53,031
52
55
139
409
479
53,646
681
696
806
54,016
202
292
341
394
500
956
55,111
104
189
218
348
468
56,137
550
717
729
969
57,473
617
731
58,065
157
58,252
413
637
59,622
664
776
61,930
63,139
274
364
564
696
64,680
65,036
66,592
828
966
976
68,273
703
757
759
703
873
69,290
516
71,243
72,431

COLON HOSPITAL CASES, 59

8,711
8,877
9,036
130
300
322
370
516
842
950
9,971
10,021
77
126
344
590
964
967
12,055
145
12,645
875
13,069
81
102
449
817
965
14,272
15,213
15,347
372
735
742
16,141
295
402
520
602
605
16,655
687
758
879
957
17,307
471
488
548
734
17,837
978
18,199
19,162
20,231
21,301
425
645
23,174
.....

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CHICAGO
AMERICAN MEDICAL ASSOCIATION
FIVE HUNDRED AND THIRTY-FIVE DEARBORN AVENUE
1911

FASCIOLOPSIS BUSSKII, F. RATHOUISI, AND RELATED SPECIES IN CHINA.

By HENRY B. WARD, The University of Nebraska College of Medicine.*

In 1843 Dr. Busk discovered a parasite which he took from the duodenum of a Lascar sailor who died in the Seamen's Hospital in London. Lankester (1857) published the original description of this parasite, which he named *Distoma Buskii.* It appears that the discoverer objected to this appellation, and in consequence when the specimen was later described by Cobbold (1860) he gave it the name of *Distoma Crassum*, a name which had been preoccupied by von Siebold in 1837 for another species of distome. Moreover, preference has no influence in scientific nomenclature, and the original specific designation must stand. Of the original specimens the majority have been lost. One which was given to Leuckart is figured in his work (1863:586). A second is preserved in the museum of the Middlesex Hospital, London, and a third in the museum of the Royal College of Surgeons. The others are in the museum at King's College, making in all only five type specimens in existence.

The second and third cases of the occurrence of this parasite were recorded in 1873 by Leidy, to whom the material was sent by Dr. J. G. Kerr, a missionary physician in Canton. Two others under the date 1875 are reported by Odhner (1902) ; the sixth case under date of 1878 by Cobbold (1879), and the seventh case under date of 1890 by Odhner (1902). This last author made a careful study of the structure of the species, which meanwhile had been assigned to the new genus *Fasciolopsis* by Looss (1899), and to him we owe our first accurate data with regard to its morphology. I have found references to cases since that date in India of which the record is inaccessible to me, and in China, reported by Heanley (1908). In addition to these Looss (1907) has examined about a dozen specimens from Hongkong, which are now in the museum of the Liverpool School of Tropical Medicine. According to Heanley these came from the pig. Finally Goddard (1904:196) reports two cases from China.

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*Presented at the Sixth Annual Meeting of the American Society of Tropical Medicine, held at the U. S. Naval Medical School, Washington, D. C., April 10th, 1909.

From correspondence with Dr. W. H. Jefferys, of Shanghai, China, who cites the opinions of others as well as his own experience in China, it seems clear that this species is far more abundant and of much greater importance than has hitherto been believed. I have myself received specimens from Dr. Jefferys, and can confirm the reports of Odhner and Looss with regard to its morphology. The characters of the genus and of the species may be outlined as follows :—

FASCIOLOPSIS LOOSS, 1899.

Fasciolinæ without anterior region clearly set off from rest of body. Cuticula smooth. Acetabulum powerfully developed with cavity extended posteriad as sacculate invagination and much larger than oral sucker. Intestinal crura simple, slender, wavy, but without evaginations. Testes dendritic with branches growing smaller towards distal ends. Cirrus pouch very long, cylindrical, containing spiral tubular seminal vesicle with peculiar cæcal appendage. Cirrus closely covered with fine spines. In alimentary canal of mammals. Type species *F. Buskii.*

FASCIOLOPSIS BUSKII STILES, 1901.

Syn : Distoma Buskii Lank. 1857 ; D. crassum Cobbold 1860 nec v. Sieb. 1837.

Length 24 to 45 mm., or even 75 mm. (Busk), usually about 30 mm.; breadth, 6 to 16 mm., usually 10 to 12 mm., maximum thickness 1.5 to 4 mm. Body moderately elongated, nearly regularly oval, ventral surface flattened, skin without spines.* Oral sucker 0.5 mm. in diameter, completely ventral ; acetabulum separated from anterior end by about its diameter, 1.6 to 2 mm. with deep triangular lumen extending caudal. Pharynx large powerful, prepharynx present. Œsophagus very short, intestinal crura slender, extending to posterior end with two characteristic curves towards the median line, one at centre of body, the other between the testes. Genital pore immediately anterior to acetabulum. Cirrus sac cylindrical, median, prominent, extending from acetabulum about half way to shell gland.

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* Odhner and most others say the cuticula is without any sort of armature, but Heanley states most positively that it has spines, whether taken from man or pig, although they are very difficult to find in some mounted specimens.

Testes, dichotomously dendritic, posterior to transverse yolk duct and in median field, one behind the other. Germarium small, dendritic, just anterior to transverse yolk duct on the right side. Laurer's canal present, but receptaculum seminis wanting. Uterus in irregular open coils anterior to ovary. Vitellaria well developed with minute acini, extending from acetabulum to posterior end, where they merge, although the band is nearly interrupted at the posterior end in the median line. Eggs very thin shelled, 120-130″ long by 75″ to 80″ broad, with minute operculum and finely granular contents. Development unknown.

Parasitic in the duodenum of man in India, Siam, China, Assam, and Sumatra, according to various authors. Very common in South China pigs (Heanley).

The presence of this parasite is said to be accompanied with high temperature (to 106° F.), bloody diarrhœa, emaciation, tympanic abdomen, edema, in general typhoid symptoms. Several of the cases have terminated fatally, owing in part at least to the late date at which treatment was sought. Calomel, thymol with castor oil or salts, and eucalyptus oil have all been used with success to expel these parasites.

It is important to note here the various records concerning the occurrence of this species in the United States, which are to be found in the literature. The first of these is given on the authority of Leidy (1891), where the parasite is listed under the name of *Distomum crassum*. As early as 1873 in fact he reported the specimens which in this later paper he places in the species named. The material, as already noted, came from Dr. J. G. Kerr, of Canton, China, and was vomited by a Chinese boy. A girl of English parents in Canton is also recorded as having passed the same parasite from the bowels. While first recorded in our literature, it should be noted that the parasites were not obtained on this continent, but were sent here for determination merely. These are the only specimens which Leidy reported from the human host.

In the same paper and immediately in connection with these specimens of *D. crassum* from man, Leidy also records that he had received specimens of this parasite from New York, Arkansas, and Texas, where they were found in the liver of a doe (N. Y.) and of cattle (Ark. and Tex.). Although Leidy says these specimens preserved in alcohol "appear to be identical with *D. crassum*," and though they have frequently been recorded under this name, yet they do not actually belong to the species under consideration. The forms in question were in reality *Fasciola magna*, a species which is now well recognized as a parasite of American herbivora.

On the other hand, the probable introduction of *F. Buskii* from the East, which I predicted in 1903, has been demonstrated in the discovery of a case by Moore and Terrill (1905). The specimen was removed at the necropsy of a Lascar sailor from an English steamer, who died at Galveston, Texas, of typhoid fever. This is the only record of the species for this continent so far as I can ascertain. With regard to their record of the parasite I wish to call attention to one error, which may be the cause of some confusion if not corrected. These authors give the average size of the ova as 150 and 75″. If the magnification assigned to their microphotographs is correct not even the largest reaches this length, and the actual size agrees closely with the measurements of Looss cited above. A similar error has been made in the case which Goddard has recently (1907:195) reported from China; the material was referred to a committee, and that part of the report of the Investigation Committee which deals with the eggs reads as follows: Eggs (possibly immature). Size not measured, about a half that of *Ascaris lumb.* Shell, very thin walled. Contents clear, small and granular, well marked nucleus in centre. Nearly spherical. No operculum observed.

An error is certainly present here, for the size of these ova would equal only 40″ to 45″ by 25″ to 30″ on the basis they give in their estimate. This is far too small for *Fasciolopsis Buskii.* If one infers that the proportions relative to *Ascaris lumbricoides* are by accident reversed in their statement these ova would approximate 130 to 150″ by 100″ to 116″, and this again fails to agree with the species *F. Buskii*, to which they assign these specimens. In fact the designation "nearly spherical" which they use to characterize the ova, cannot by any means be applied to the figure which Looss gives of ova in *F. Buskii.* Renewed investigations alone can tell whether the authors are in error as regards their measurements and description or with respect to their identification of the species.*

Recently Barrois and Noc (1908) have reported this species as frequent in Cochin China. Among 133 Annamite prisoners, coming from various provinces, 16 were found, on systematic treatment with thymol, to be carriers of *F. Buskii.* In thirty-six autopsies, however, not a single case of infection with this species was discovered. Among the sixteen cases infected the flukes were solitary in five instances; three parasites were present in each of three cases; four, five, six, seven, and twenty-four parasites were found in one case each, and finally even thirty-six flukes in one case. It is worthy of note that Barrois and Noc think this parasite of little or no consequence unless present in large numbers. In this opinion they are at variance with other observers, whose opinions are already cited.

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*Note.—The species was F. Buskii without shadow of doubt. The conclusions with regard to the eggs were erroneous and have been already retracted and corrected, as far as possible, by the reporters. The report was merely preliminary to submitting the matter to specialists.—Editor.

These authors also record the size of the parasite as 25 to 70 mm. in length by 6 to 12 mm. in breadth and 1.5 mm. in thickness. It is longer, they continue, than *Fasciola hepatica*, of which it has not the leaf-like form, but may be most easily distinguished at a glance by its considerable thickness. As regards anatomical details they merely confirm in general the description of Odhner (1902) with the difference that the ovary and shell gland, in place of being situated at the middle of the body as he indicates, are located about at the union of the anterior and middle third of the body.

In 1887 Poirier described as *Distoma Rathouisi* a new human parasite from a single specimen sent him from China by the Reverend Father Rathouis. According to the record the fluke was passed by a Chinese woman, thirty-five years of age, at the mission Zi-ka-wei. The woman had suffered long from hepatic pains, which were not amenable to treatment. Hence Poirier concludes that the specimen came from the biliary ducts. Poirier gives an extended description of the anatomy which he compares in detail with *D. hepaticum*, the well-known liver fluke, common through Europe in sheep and occasionally also found in man.

For twenty years after its discovery and description Poirier's species was not reported again. Many authors, among whom Leuckart, only need be noted, inclined to the view that it was identical with *Fasciolopsis Buskii*, originally reported from India. When the latter species was carefully studied by Odhner his work showed that the two forms were in all probability not identical. A careful examination of the records also indicated to me their evident relationship. Accordingly in a revision of human trematode parasites I (1903) included Poirier's forms as a distinct species in the genus *Fasciolopsis*. Of Odhner's most recent paper (1909) I shall speak later.

Recently Goddard (1907) reported from Shaohsing, China, two cases of its occurrence. In the first, a woman forty-two years age, there was a mixed infection with *F. Buskii*. After the administration of eucalyptus oil, chloroform, and castor oil, specimens of both parasites were passed on three successive days. The patient was greatly emaciated, and treatment was delayed so long that she died. An autopsy was impossible. In the second case, a boy six years old, the eggs were found in the feces, and administration of eucalyptus oil, as before, brought away many parasites at intervals of two or three days. Two weeks later two specimens were vomited. The patient is still under observation.

According to Goddard the parasite is common in that region and is thought usually to cause death. The cardinal symptoms are enlarged abdomen, diarrhœa, wasting, and occasionally jaundice. The stools are usually light yellow in color and of a peculiarly offensive odor. Goddard observed under the microscope groups of bile-stained cells resembling lives cells ; sometimes with no definite outline, sometimes three or four lobules held together by the enclosing net work of fibrous tissue. Yet he observed no symptoms of liver involvement. Other cases of the disease are under observation.

The specimens from these cases were submitted to Drs. J. L. Maxwell and W. H. Jefferys, of the Research Committee, who say that the specimen appears to be *Distomum Rathouisi*, though the description of this worm on record differs in some particulars from their observations. They had at the same time specimens of *Fasciolopsis Buskii* from the other case and note emphatically that they "dissent altogether from the statements of Scheube that these two distomata are varieties of the same worm. In our specimen their form, size, and consistency differ in many particulars." The ova are important factors in determining a parasite fluke. Goddard's account of these structures is as follows : The eggs of the *D. Rath.* are about two-fifths of the microscopic field under a one-sixth inch objective and one inch ocular, have a thin shell and appear to possess a hyaline body moderately well filled with coarse granules of a greenish yellow tint (? in fresh feces). These eggs were present in both cases reported (one was a case of mixed infection with *F. Buskii*, and the figures given in this report show a difference in size of the ova).

The report of the Investigation Commitee, to whom these specimens were submitted, is given in the same paper (Goddard 1907:198). The description of the ova reads thus : Eggs, oval, size not measured, about one-third larger than *Asc. lumbric.* Thin walled and smooth with very small operculum. Contents appear to consist of large granules.

I have discussed the records of this species in a recent paper (1908). "From Goddard's account the size of the ova may be estimated as approximately 100-115″ by 65-75″. Such an ovum would be very much smaller than that described by Poirier for his *Distomum Rathouisi.* The Investigation Committee notes in its report some doubt as to the correctness of the identification, and the doubt is emphasized by this discrepancy in the size of the ova. Further study of these forms is needed to establish their true character."

Since writing the above account through the great kindness of Dr. Jefferys, I have received three specimens of this parasite, of which he writes :—

> "The other worm, of which I can spare you two specimens, is less certain. Maxwell (Tainan, Formosa) believed it to be *Distomum Rathouisi*, and I think it possibly is so, though I felt doubtful as he, too, does now. If the testicles of *Distomum Rathouisi* are right and left, then this is not that worm. Otherwise it corresponds to such descriptions as given in Braun, for instance. Anatomically it is much like *Fas. Buskii* and appears in the same patients at times. There are these few differences : it is shorter and thicker in proportion, and this factor is constant, that is, if the stool has both kinds of worms, it is easy and simple to place each worm present in one or the other group. It is more regularly oval and does not have wavy edges or lean to one side. (See also Goddard's report.) As you know, there has always been a doubt as to whether or not these two worms are the same or different. Personally I am inclined to believe they are the same and that the original description of *Distomum Rathouisi* was faulty with regard to the position of the testicles. Possibly a difference in date of infection might account for the difference in size, but why can we not have a large breed of worms and a small, as a large breed of horses and a small?"*

Again in October, 1908, Dr. Jefferys sent me another lot of the same species ; there were nine specimens, which he writes were obtained by Goddard, but gives no further data. At the same time he sent a batch of five flukes labeled "Probably *Rathouisi* also, passed with last. Seem different to naked eye. Have just acquired and not cleared any yet."

From this material I have been able to make an extended study of this species. The original description of Poirier is in error at many points, but this is not strange in view of the fact that he only had a single specimen at his disposal. The results of my work may be summed up in the following specific diagnosis.

FASCIOLOPSIS RATHOUISI WARD, 1903.

Syn. Distomum Rathouisi Poirier, 1887.

Length 15 to 19 mm., breadth 8.5 to 10.5 mm., thickness up to 3 mm., shape bluntly oval or elliptical, with short cephalic cone, sharply marked off from body in profile aspect only and usually bent ventrad and even slightly posteriad. Alcoholic specimens light grayish brown, sometimes darker. Usually flexed with dorsum concave and

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*It is interesting to note how the observer after having noted and recorded clearly the differences in external appearance between the two species is led at the close of his report to question their specific identity on the basis of an argument often advanced and very specious, yet thoroughly fallacious. The fallacies of this argument are so well exposed by Looss in various papers (1899, 1907, *et alia*) that it would not be profitable to go into them here. I have myself recently (1908) discussed the question with especial reference to the ova and have shown some of the errors which have followed in the past from the assumption of a position such as suggested by Dr. Jefferys. Closely related species of flukes are continually interchanged and the errors in determination resulting therefrom have led in the past to great confusion.

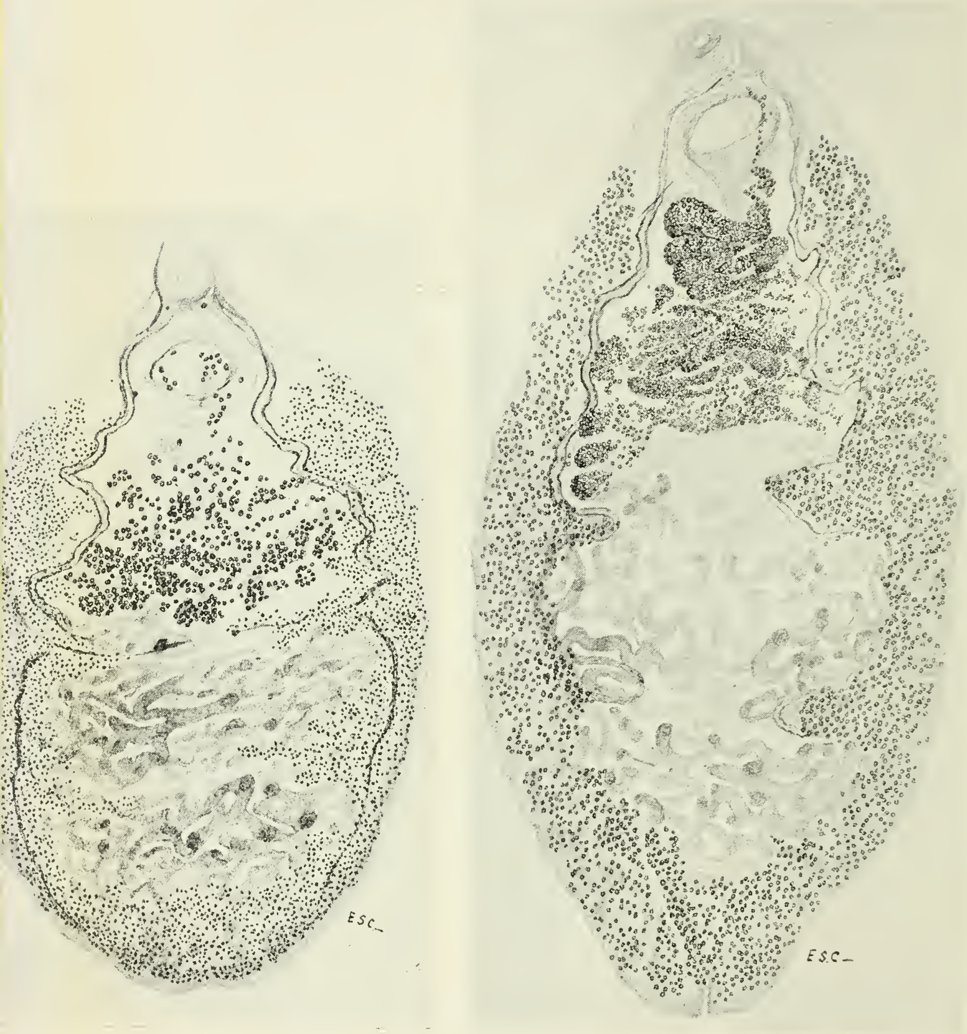
edges only very slightly crenate, if at all. Oral sucker small, subterminal 0.25 to 0.29 mm. broad by 0.2 mm. in antero-posterior diameter, with cavity looking ventrad, separated from ventral sucker by about twice its own diameter. Acetabulum 1.32 to 1.38 mm. broad by 0.68 to 0.7 mm. in antero-posterior diameter. Œsophagus almost lacking. Internal organs much as in *F. Buskii* except in detail. Some more prominent items noted here. Intestinal crura somewhat more irregular and probably with more and more pronounced curves. Cirrus sac not conspicuous as in *F. Buskii.* Testes more compactly branched, broader and denser than in *F. Buskii*, posterior to transverse yolk duct and in median field. Contrary to the report of Poirier they lie one behind the other. Germarium on right side, small, coarsely branched. Uterus in broad, heavy, closely grouped coils, anterior to ovary. Vitellaria outside of intestinal crura from about level of acetabulum to posterior end, where they merge without indication of interruption. Masses of acini also drift over intestinal crura towards centre of body at several places. Eggs oval, thin shelled, with delicate operculum.

Concerning *F. Rathouisi* in China and its effect on the host Goddard (1907) writes as follows:—

> This parasite, known to the Chinese as Siau San Dzoong, is quite common here and is thought usually to cause death, because the Chinese remedy is so obnoxious to the patient that the parents (for patients are usually children) are too sympathetic to make them take it. The cardinal symptoms are enlarged abdomen, diarrhœa, wasting and occasionally jaundice. The appetite is usually preserved. The cause is supposed to be the excessive eating of aromatic foods, such as peanuts, or more especially the eating and drinking of all kinds of things at all kinds of times, thus preventing digestion. This produces the worm, so say the Chinese. I am inclined to think the egg may be carried on uncooked vegetables or raw fruit, but thus far have failed to find it.
>
> The relation of this disease to the liver is interesting. The stools are usually light yellow in color and of a peculiarly offensive odor. Under the microscope I have found groups of bile-stained cells resembling liver cells; sometimes with no definite outline, sometimes three or four lobules held together by the enclosing network of fibrous tissue. Clinically I have observed no symptoms of liver involvement.
>
> Several other cases of this disease are now under observation and will be reported later on.

To the original case reported by Poirier may be added the two noted by Goddard, and one, sent me by Jefferys in 1908 as noted above, which also comes from Goddard. Two of these are mixed infections; the one of Goddard (1907) being complicated by *F. Buskii* and the last case noted having, as Jefferys writes, another form, of which more later.

Within a very short time I have seen a paper by Odhner (1909), in which after an examination of Poirier's original specimens from the



(Both figures drawn from life to same scale.)

Adult of Fasciolopsis Rathouisi.

Adult of Fasciolopsis Goddardi.

Paris museum, he endeavors to demonstrate that *D. Rathouisi* represents a contracted specimen of *F. Buskii.* He rightly points out some errors in the original description of *F. Rathouisi*, which include some items given in the above synopsis, and yet I cannot possibly share his conclusions. Several good observers in China, among them Jefferys, Goddard, and Maxwell (v. a) note the differences in the appearance of the living specimens. They are equally easily distinguished in the alcoholic material. The form differs radically and is constant. The surface is not wrinkled as it would be if noticeably contracted ; there is a sort of cephalic cone here which is absent in *F. Buskii.* The uterine coils are more frequent and more filled with ova. The acini of the yolk gland are more numerous and somewhat differently distributed. The suckers are not precisely alike in size, though more nearly so than indicated in Poirier. In short the differences, while slight, are sufficient to constitute the two forms of different specific rank, and *F. Rathouisi* is undoubtedly a good species.

Among the specimens forwarded to me by Dr. Jefferys in October, 1908, were five, which he noted as being different to the eye from *F. Rathouisi*, although they were passed with the batch of that species sent me at the same time. They were somewhat larger than *F. Rathouisi*, measuring 21 to 22 mm. in length by 9 mm. in width. The general aspect is of a larger and slenderer worm, and the light yellowish gray color of the alcoholic specimen enables one to pick them out at a glance. At first thought they appeared as transitional forms between *F. Rathouisi* and *F. Buskii* and likely hence to establish the identity of those two forms which has been maintained, but further examination revealed the improbability of this view. The oral sucker is somewhat smaller, the testes different in form and the uterus much more closely coiled. Even if one may suppose that all of these differences are produced by varying contraction, there yet remains a conspicuous difference in the size of the yolk gland acini, which is very striking and apparently beyond modification by contraction or other change in form. It may be that this form represents merely an older specimen of *F. Rathouisi*, but reference to Odhner's figures will show at once that it can hardly be a younger or less developed form of *F. Buskii* since it is in every way fully developed. I am inclined to consider it a new species, to which the name *F. Goddardi* may be given.* There is hardly opportunity here to discuss the matter in detail. I expect to consider it most extensively in a larger paper on these forms now under preparation.

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* NOTE.—As the JOURNAL goes to press, Dr. Jefferys has received two typical specimens of F. Goddardi from Dr. Garner, of Shanghai, which she reports as having been vomited by a Chinese boy.—EDITOR.

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THE SPUTUM OF TYPHOID FEVER PATIENTS AS A POSSIBLE SOURCE OF INFECTION.*

BY ELMER S. TENNEY, B.L., M.D., U. S. ARMY, FORT STRONG, MASS.

(From the Department of Preventive Medicine and Hygiene, Harvard Medical School.)

At the suggestion of Dr. Rosenau, and with his kind advice and assistance, I have been able to carry out the following study of the saliva and sputum of 53 cases of typhoid fever.

Thanks are due to Dr. MacCollom, superintendent of the Boston City Hospital; to Dr. Washburn, superintendent of the Massachusetts General Hospital, and to Dr. Lucas, of the Children's Hospital, for kindly placing at my disposal the cases of typhoid occurring at these hospitals during the past winter.

So far as I am aware from a careful examination of the available literature, very little of a definite nature has been published in relation to the infectiousness of the saliva and sputum of typhoid fever patients. In reviewing the literature the impression one gets is that the bacillus typhosus is not frequently to be found in the mouth; that it may be, but usually is not, the cause of pneumonia complicating typhoid fever; and that while thus rarely to be found in the mouth, still, because it may be found there, the saliva and sputum should be treated as a possible source of infection.

No writer except Richardson whom I have consulted makes any definite statement that he has himself done any experimental work upon the subject or quotes the writings of any one who has. To give an idea of what seems to be the opinions most commonly held upon the subject, I will refer briefly to the expressions of a few writers.

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* Read by title at the annual meeting of the American Society of Tropical Medicine at St. Louis, June 11, 1910.

Osler and also Field seem to think that the typhoid bacillus is to be found in the mouth more frequently than the majority of writers. In the latest revised edition (1909) of his " Practice of Medicine," Osler says, " They are reported to have been cultivated from the sweat, and they undoubtedly occur with considerable frequency in the sputum (Richardson, Raw and others)"; he further says, " They are also present in the esophagus and on the tongue and tonsils."

The work of Richardson referred to by Osler was published in the BOSTON MEDICAL AND SURGICAL JOURNAL, in 1903, and is as follows, " As to the presence of the typhoid bacillus in the sputum, I was able, in 1897 [*Journal of the Boston Society of Medical Sciences,* Nov. 16,1897], to isolate this organism on three successive days from the sputum of a case of typhoid fever complicated with pneumonia. In 15 cases with no pulmonary complications the results were negative. Since 1897 the subject has been investigated by a few observers only. Their results show that the typhoid bacillus may be present in the sputum during typhoid fever, especially if there be a coincident bronchitis or pneumonia. The typhoid bacilli are almost invariably associated with other organisms, such as the pneumococcus or the influenza bacillus, and are to be regarded rather as secondary invaders than as the primary cause of the complication. The sputum in these cases is generally hemorrhagic and may contain large numbers of bacilli for considerable lengths of time. Seven weeks is the longest period of persistence recorded. The subject needs much further study, but enough is known to show that in the typhoid sputum we have still another excretion which must be carefully disinfected."

Under the heading of the " Distribution of the Typhoid Bacillus in the Body," Field says, " The finding of the typhoid bacillus by Besson in the tonsils of 6 out of 10 cases investigated warrants the belief that they also exist in the mouth." Jordan, in his " Textbook on Bacteriology," says, " Typhoid bacilli have been found occasionally in the sputum, although the majority of cases of pneumonia that occur during the course of typhoid fever are apparently caused by the pneumococcus. There is hence a possibility that typhoid fever may be spread by sputum infection, but it seems rather remote." Whipple states that " in some cases bacilli are found in the mouth and throat; consequently the saliva may contain them. This condition may be infrequent, but it is always liable to occur. There is practically no danger to be feared from the quietly exhaled breath, as bacteria do not readily leave a moist surface; but coughing or sneezing may cause the expulsion of the bacilli into the atmosphere, with consequent danger to persons in the room who may inhale them." Tooth, writing of his observations in the South African War, in " A Civilian War Hospital," 1901, makes the following statement: " In a tentful of men, apparently equally ill, one may almost pick out the enteric cases by the masses of flies that they attract. . . . The moment an enteric patient puts out his tongue, one or more flies settle on it." It might be inferred from this remark of Tooth's that he thought flies could thus become infected. Rosenau, in his work on " Disinfection and Disinfectants," says that " the bacillus of typhoid fever is eliminated from the body in the stools, the urine and sometimes in the sputum." In 1897 J. C. Wilson, writing in the "American System of Practical Medicine," was of the opinion that "by far the largest proportion of the bacilli are without doubt destroyed within the body. The remainder find their way out in the stools, to a slight extent in the urine, very rarely in the vomited or expectorated matters, or the perspiration. They are not eliminated by the expired air. . . . . Croupous pneumonia is, however, in some instances apparently due, not to infection by the diplococcus of pneumonia, but to infection by the bacillus of Eberth. Under these circumstances it usually occurs early in the course of the attack, and has been attributed to localization of the specific process. The difference between the two forms, however, is rather a bacteriological than an anatomical one." In a case of mine in the Jefferson Hospital, Coplin found Eberth's bacillus in the pulmonary exudate. H. W. Hill, of the Minnesota State Board of Health laboratories, says, "All our forms of outbreaks are merely the result of the following, by typhoid infected feces chiefly, but also by typhoid urine and saliva. . . ." To quote again from Jordan's "Bacteriology," "The actual evidence in favor of the invasion of the body through the tonsils and gastric mucosa is by some investigators thought to be quite as strong as the evidence of intestinal penetration." Kolle and Hetsch, in "Die Experimentelle Bakteriologie und die Infectionskrankheitens," say that the typhoid bacillus is rarely to be found in the mouth or sputum. On Dec. 20, 1909, at a meeting of the Medical Association of the Greater City of New York, as a part of a "Symposium on the Throat Symptoms of General Diseases," Dr. Coffin discussed the laryngeal complications of typhoid fever, calling attention to the fact that the larynx is much more frequently involved in some localities than in others, and most often in the severer epidemics. He quoted a paper by Drs. Jackson and Day, of Pittsburg, written some years ago, in which they reported that " of 360 cases that were carefully watched throughout the course of the disease, 227 showed lesions in the larynx." Of these cases, he said that some showed simply a subacute laryngitis, others a laryngitis with an ulceration of the mucous membrane, while in the more severe cases the cartilages and pericartilaginous tissues were involved.

Following Dr. Coffin, Dr. Nathan B. Van Etten said that " the uvula, tonsils and pharynx were often ulcerated, and, in cultures from these ulcers, typhoid bacilli had often been obtained. The frequent finding of the bacilli in the sputum indicated the necessity of the destruction of all mouth secretions as sources of infection." (The quotations above are from the " Society Reports " in the *Medical Record* of March 12, 1910, page 465.) That every victim of typhoid fever must receive his infection through the mouth is an admitted fact; ordinarily this occurs through the introduction of food or drink, the greater part of which passes directly to the stomach, but it is not unreasonable to suppose that small contaminated particles may find lodgment upon the teeth and gums, where, if conditions be right, they should readily multiply. The saliva usually has a weak alkaline reaction which makes it, so far as that point is concerned, suitable for the growth of the typhoid bacillus, and as the result of actual trial I have found that it will readily multiply in it. If, then, the infecting bacilli must first pass through the mouth to reach the blood stream, and if the saliva in the mouth is a suitable medium for its growth, why should the bacillus not be found in the saliva in sufficient numbers to be demonstrated with the proper technic and, of course, be a possible source of danger to others? It was with the idea of determining, if possible, the above question that this work was begun. It was further hoped that, in addition, something might be learned as to its frequency at the different stages of the disease. The work was begun in the autumn, but not completed until the following spring, owing to the scarcity of material. As the list of the tabulated cases which follows will show, material was obtained from cases as early as the fourth day of illness and as late as the seventieth; specimens were secured from seven cases several days before a positive Widal reaction could be obtained.

The material studied consisted of the expectoration, collected in the ordinary sputum collecting bottles in use by the Boston Board of Health; and, in addition, material was collected on ordinary diphtheria swabs from the tonsils, the surface of the tongue, the gums and any carious teeth that might happen to be present.

These specimens were invariably brought to the laboratory within one hour of the time of collection, diluted with about four parts of normal salt solution and then thoroughly shaken and mixed; it was allowed to stand while the culture medium was being prepared and again shaken before the plates were inoculated.

The medium used was Endo's fuchsin agar, made after the modification recommended by the Hygienic Laboratory at Washington (see Hygienic Laboratory Bulletin, No. 52, October, 1909, Report No. 3, on "The Origin and Prevalence of Typhoid Fever in the District of Columbia," 1908, by M. J. Rosenau, L. L. Lumsden and

Joseph H. Kastle), which are as follows: " Make 4% neutral agar as follows: Take 1 liter distilled water, add 5 gm. sodium chloride, 10 gm. Liebig's extract meat, 10 gm. peptone. Dissolve by heating, allow to cool, and place on surface 40 gm. powdered agar.

" When this has settled, place in Arnold sterilizer, covering beaker with paper, and cook for three hours.

" Filter through cotton on a perforated funnel (*Büchnerfilter*) by the aid of a vacuum, or allow to settle while slowly cooling and discard the bottom turbid portion.

" Neutralize to litmus paper with Na_2CO_3 solution. Add 10 ccm. sterile 10% Na_2CO_3 solution.

" It is convenient at this point to put up the medium in 100, 200 and 400 ccm. quantities in flasks, the flasks being large enough to provide room for the other ingredients.

" These can be stored until needed for use; the agar is melted and the other ingredients added in the proper proportion.

" Add 5 ccm. alcoholic fuchsin solution. This is prepared as follows: To 10 gm. fuchsin (not acid fuchsin) add 100 ccm. 96% alcohol, shake, allow to stand twenty hours, and filter the supernatant fluid which is used. It should be filtered each time before using.

" Add 25 ccm. freshly made and sterilized 10% sodium sulphite solution.

" Sterilize for a few minutes in the Arnold and pour plates while the medium is steaming hot.

" The medium after cooling should be nearly colorless to transmitted light and rose or flesh-colored to reflected light.

" The lactose, fuchsin and sodium sulphite solutions must be added to the melted agar just before it is to be used.

" The plates are flown and allowed to stand for twenty minutes (my plates were given one hour) uncovered in the incubator in order to do away with the water of condensation and to obtain a good surface.

" Organisms which split lactose restore the red fuchsin and appear as deep red sharply limited opaque colonies with a greenish surface sheen.

" The typhoid organism produces smaller transparent colonies resembling a small drop of water."

The plates were inoculated with a sterile glass rod which had been bent at a right angle, the short arm being dipped into the thoroughly mixed material in the salt solution and then rubbed firmly and evenly over the surface of the plate and successively over a second and third in order to get the necessary distribution of colonies. The plates were incubated at 37° C. for twenty-four hours, and then subcultures in plain boullion were made from all suspicious-looking colonies. Each tube of plain boullion containing about 4 ccm. was incubated for twenty-four hours, after which a small drop of Parke, Davis & Co. typhoid serum was added, making a dilution of not far from 1 to 400. This serum when tested against a laboratory culture of typhoid which I isolated about one year ago showed marked agglutination in fifteen minutes in dilutions of 1 to 1000, and quite perceptible clumping in less than two hours in dilutions of 1 to 2500. The tubes were examined after one hour and the results recorded, but all were allowed to stand for twenty-four hours and again examined, at which time, if any tube showed what appeared to be a partial agglutination, it was put aside for further study. Whenever material was obtained upon swabs, after the Endo plates had been inoculated, the swabs

Specimens of Saliva and Sputum Examined for Typhoid Bacilli.

Case.	Age.	Sex.	Day of disease.	Swab.	Sputum.	Times examined.	Widal reaction.	Serum reaction.	Remarks.
1	20	F	35	1	1	1	*	—	Bronchial symptoms
2	19	M	38	1	1	1	*	—	Bronchial symptoms
3	22	M	18	1	1	1	*	—	Bronchial symptoms
4	35	F	49	1	1	1	*	—	
5	19	F	46	1	1	1	*	—	*Blood culture
6	25	F	46	1	1	1	*	—	
7	10	M	49	2	2	2	*	—	
8	28	M	14	2	2	2	*	—	Bronchial symptoms
9	18	M	59	2	2	2	*	—	Relapse; bronchial symptoms
10	25	M	28	1	1	1	*	—	Relapse
11	20	M	14	1	1	1	*	—	
12	12	F	9	2	2	2	*	—	
13	10	F	10	1	1	1	*	—	
14	10	M	10	2	0	2	*	—	
15	9	M	10	2	2	2	*	—	
16	32	M	10	1	1	1	*	—	Bronchial symptoms
17	20	F	60	0	1	1	*	—	
18	10	M	9	2	2	2	*	—	
19	21	M	40	1	1	1	*	—	
20	20	F	20	1	1	1	*	—	
21	20	M	28	1	1	1	*	—	
22	25	F	53	1	1	1	*	—	
23	12	F	14	1	1	1	*	—	
24	28	F	28	1	1	1	*	—	
25	25	M	70	1	1	1	*	—	
26	15	F	14	0	1	1	*	—	
27	27	F	70	0	1	1	*	—	
28	20	M	14	2	2	2	*	—	Bronchial symptoms
29	15	F	36	0	1	1	*	—	
30	5	F	50	1	0	1	*	—	
31	6	F	35	1	0	1	*	—	
32	25	M	24	1	0	1	*	—	
33	40	M	35	1	0	1	*	—	
34	6	M	28	1	0	1	*	—	
35	28	M	5	0	2	2	*	—	
36	16	F	4	1	0	1	*	—	
37	9	F	56	1	0	1	*	—	
38	4	M	62	2	0	2	*	—	
39	26	M	16	2	2	2	*	—	
40	48	F	40	0	1	1	*	—	Bronchial symptoms
41	7	F	27	1	0	1	*	—	
42	9	F	28	1	0	1	*	—	
43	20	F	11	2	0	2	*	—	
44	26	F	15	0	1	1	*	—	
45	30	F	6	0	1	1	*	—	
46	19	M	25	0	1	1	*	—	
47	30	M	15	0	1	1	*	—	
48	38	M	30	0	1	1	*	—	
49	26	F	20	1	0	1	*	—	
50	13	F	55	1	0	1	*	—	
51	17	M	35	1	0	1	*	—	Bronchial symptoms
52	18	M	7	1	0	1	*	—	
53	21	F	14	1	0	1	*	—	

The sign * stands for positive in this paper.

Control Specimens of Saliva and Sputum, of Known and Unknown Origin, Examined for Typhoid Bacilli.

No.	Name.	Age.	Serum reaction.	Remarks.
1	“ A ” unknown	Fresh	*	Colonies typical
2	“ B ” unknown	Fresh	—	Colonies not typical
3	“ T ” known	Fresh	*	Colonies typical
4	“ C ” unknown	Fresh	*	Colonies typical
5	“ D ” unknown	Fresh	*	Colonies typical
6	“ E ” unknown	Fresh	—	Colonies not typical
7	“ F ” unknown	Fresh	*	Colonies typical
8	“ G ” unknown	Fresh	*	Colonies typical
9	“ H ” unknown	Fresh	—	Colonies not typical
10	“ C ” No. 4	7 days old	*	Colonies typical
11	“ D ” No. 5	7 days old	*	Colonies typical
12	“ F ” No. 7	7 days old	*	Colonies typical
13	“ G ” No. 8	7 days old	*	Colonies typical
14	“ X ” known	Fresh	*	Colonies typical
15	“ C ” No. 4	21 days old	*	Colonies typical
16	“ D ” No. 5	21 days old	*	Colonies typical
17	“ F ” No. 7	21 days old	*	Colonies typical
18	“ C ” No. 8	21 days old	*	Colonies typical
19	“ X ” No. 14	13 days old	*	Colonies typical
20	“ X ” No. 14	18 days old	*	Colonies typical
21	“ X ” Transplant	Fresh	*	Colonies typical

22	“G” No. 8	38 days old	*	Colonies typical
23	“X” Transplant	7 days old	*	Colonies typical
24	“D” No. 5	43 days old	*	Colonies typical
25	“X” Transplant	17 days old	*	Colonies typical
26	“X” Transplant No. 2	Fresh	*	Colonies typical
27	“C” No. 4	61 days old	*	Colonies typical
28	“D” No. 5	61 days old	*	Colonies typical
29	“G” No. 8	61 days old	*	Colonies typical
30	“X” No. 14	53 days old	*	Colonies typical
31	“X” Transplant	35 days old	*	Colonies typical
32	“X” Transplant No. 2	18 days old	*	Colonies typical
33	“C” No. 4	84 days old	—	Colonies not typical
34	“D” No. 5	84 days old	*	Colonies typical
35	“F” No. 7	84 days old	*	Colonies typical
36	“G” No. 8	84 days old	—	Colonies not typical
37	“X” No. 14	76 days old	*	Colonies typical
38	“X” Transplant	58 days old	*	Colonies typical
39	“X” Transplant No. 2	48 days old	*	Colonies typical
40	“X” No. 14	113 days old	*	Colonies typical
41	“D” No. 5	125 days old	*	Colonies typical
42	“F” No. 7	125 days old	—	Colonies not typical
43	“X” Transplant	95 days old	—	Colonies not typical
44	“X” Transplant No. 2	85 days old	—	Colonies nearly typical
45	“X” Transplant No. 3	41 days old	—	Colonies nearly typical

were used to inoculate lactose boullion fermentation tubes, from which additional Endo plates were made the following day; and all suspicious colonies on these plates were treated in the same manner as above, as it was thought that by this enriching process the bacilli might be discovered in cases where they were only present in small numbers. It was found that only a small number of the organisms occurring in the mouth will grow on Endo's medium and that every one of these has a more or less distinctive appearance in colonies to distinguish it from colonies of typhoid or other members of the typhoid group. In nine of these cases there were bronchial symptoms, but in none was there a case of pneumonia; it was not observed that there was any variation in the varieties grown from these and those without such symptoms. No throat complications, such as described by Drs. Coffin and Van Etten, were noticed in any of this series.

The work was controlled in the following manner. A plate inoculated with a laboratory culture of typhoid bacilli was always made as a check on each batch of medium throughout the work; and during the early part, in order to test out the whole technic, ten specimens of saliva and sputum, two of which (" T " and " X") were known to have been inoculated with two loopfuls of an agar typhoid culture and eight of which were prepared by other persons and about which nothing was known to the writer. The colonies of each of the " unknowns " were so typical that, in every instance, I was able to pick those containing typhoid bacilli before resorting to the serum agglutination test, which I did later to confirm my opinion. Finding that my technic appeared to be satisfactory, I turned these "control cultures" to a new purpose by making Endo plates from those which were positive, at intervals, in order to ascertain if the bacilli would keep alive in the sputum for any considerable length of time. As the chart shows, all were alive at the end of sixty-one days, but "C" and "G" were not alive at the end of eighty-four days, or at least, if typhoid bacilli were still present, they were not demonstrable with the technic employed. Plates from those two specimens showed colonies resembling the ordinary typhoid colonies somewhat, but inclined to be more opaque, and did not agglutinate. In order to find out if saliva and sputum makes a suitable medium for the growth of typhoid bacilli, I made transplants from specimen "X," when it was twenty-one days old, into fresh saliva and sputum (this became "X transplant"), and sixteen days later I transplanted this into still another fresh specimen of the same material, which became "X transplant No. 2." Thirty-eight days later I inoculated another fresh lot of material from "X transplant No. 2," which thus became "X transplant No. 3." All of these subcultures were plated out on Endo's medium in the same manner as the specimens obtained from typhoid patients, and each gave a positive reaction when tested with the typhoid serum. Usually after the inoculated specimens were three weeks old, the plates showed very little beside typhoid colonies, the other organisms which were present on the plates made from the freshly inoculated saliva and sputum being apparently less resistant. In transplanting from one specimen to another one loopful of the old was added to about 4 ccm. of the material; these were always left in the laboratory at room temperature.

SUMMARY.

In a study of the saliva and sputum of 53 cases of typhoid fever, several of which showed bronchial symptoms, but none pneumonia or any laryngeal complications, the bacillus was not found by means of the technic employed.

Typhoid bacilli will live for at least one hundred and twenty-five days in the saliva and sputum and can be readily transplanted from one specimen of such material to another and kept growing in it at room temperature for a long time.

CONCLUSIONS.

The examination of this limited number of cases shows that, in those uncomplicated by pneumonia or by laryngeal inflammation, the typhoid bacillus is not frequently found in the mouth.

In view of the reported finding of the bacillus in cases complicated by pneumonia and by laryngeal inflammation, it would seem that more work, especially upon cases showing these symptoms, should be done along the lines followed in this series.

While the sputum does not frequently contain the typhoid bacillus, it does so occasionally, and on that account it cannot be ignored as a source of infection.

A STUDY OF THE TYPE OF INFANTILISM IN HOOKWORM DISEASE*

ISAAC IVAN LEMANN, M.D.
NEW ORLEANS

A search of the literature has shown that no one has yet given more than cursory notice to the striking infantilism of hookworm disease. So striking is the phenomenon that authorities have contented themselves with mentioning its existence as a well-known fact. The subject is dismissed with the general statement that hookworm victims are undersized, lack pubic and axillary hair and show other evidences of lack of development.

It is the purpose of this paper to report in detail the exact study of the grade of development in a case of hookworm disease and, by contrasting it with other types of infantilism, to endeavor to fix its classification.

Personal History.—O. J., a white male, aged 22, from Biloxi, Mississippi, was admitted to the Charity Hospital, April, 1909, for treatment for anemia secondary to hookworm infection. He had ground-itch for the first time when he was 6 years old and had it every summer until he stopped going barefoot at the age of 19. He has not grown since he was 12 years old. From his tenth year he used to "bloat up" and did not feel like going about. This lasted for five or six years, but from his sixteenth year he has been pretty well except that he tired easily. He attended school off and on from the time he was 5 years old—altogether for perhaps three years. When he left school at 14 he was in the seventh grade. He had no difficulty with his lessons and always stood near the top of a class of from ten to twenty-five. At 17 he was sick a whole summer with fever, which was diagnosed as malaria. He had measles at 14 and mumps at 21. The diagnosis of uncinariasis was made by a physician who was called to see him because of a slight cold. He was first treated at the Touro Infirmary in November, 1907, and felt a great deal better after his treatment there. He returns now for treatment because he fatigues easily. He has lived at various times in the following places (all in Mississippi): Biloxi, Pass Christian, Orrisburg, Poplarville, Hattiesburg.

Family History.—The father died of typhoid, but the mother is living and well. One brother is living and well, 20 years old, weighs 160 pounds; he has had ground-itch a few times. Two sisters, 17 and 20 years old, respectively, are living and well. Each weighs 115 pounds. Neither has had ground-itch. The patient says that his brothers and sisters are well developed.

Present Condition.—The patient is a small, pale, sallow individual, apparently about 13 or 14 years old. His intelligence is good. His answers are quick, his skin is dry, his hair is thick and coarse and there are areas of alopecia over the occiput.

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*From the Clinic of Prof. George Dock, Tulane University of Louisiana.

Thorax: Heart not enlarged; no murmurs. Lungs normal.

Abdomen: No distention. Liver is not enlarged.

Spleen is not palpable. Slight tenderness on pressure over the epigastrium.

Wing scapulæ.

No axillary or pubic hair.

Genitalia correspond in size and development to apparent age of patient.

The following blood-picture (made May 10, 1909) is representative of a number of blood examinations made from time to time:

Hemoglobin, 45 per cent.; red blood cells, 4,160,000 to the c.mm.; leucocytes, 7,600 to the c.mm. Eosinophils, 9⅔ per cent.

Examination of stools showed ova of uncinaria still present.

Measurements:

Skull:

Fronto-occipital circumference, 53.5 cm.
Mento-vertical circumference, 57 cm.
Mento-occipital circumference, 61 cm.

Chest:

Full inspiration (at nipple level), 70.25 cm.
Full expiration (at nipple level), 63.75 cm.
Full inspiration (at level of armpits), 63.5 cm.
Full expiration (at level of armpits), 58.5 cm.
Full inspiration (at base of chest), 64.75 cm.
Full expiration (at 8th rib), 58 cm.

Height standing, 139.5 cm.

Distance from umbilicus to the ground, 85 cm.

Distance from the tip of his fingers (placed on his thigh while standing) to the ground, 54.5 cm.

Upper extremity:

Acromion to olecranon, left, 27.5 cm.; right, 27 cm.
Olecranon to tip of middle finger, left, 37 cm.; right, 37.25 cm.
Ulna, left, 22 cm.; right, 22 cm.

Hands:

Thumb (right) metacarpal, 5 cm.: first phalanx, 2 cm.; second phalanx, 2.5 cm.; (left) metacarpal, 5 cm.; first phalanx, 2.5 cm.; second phalanx, 2 cm.

First finger (right) metacarpal, 7 cm.; first phalanx, 3.25 cm.; second phalanx, 2.5 cm.; third phalanx, 1.5 cm.; (left) metacarpal, 7 cm.; first phalanx, 3.5 cm.; second phalanx, 2.5 cm.; third phalanx, 1.5 cm.

Second finger (right) metacarpal, 7 cm.; first phalanx 4 cm.; second phalanx, 3 cm.; third phalanx, 1.5 cm.; (left) metacarpal, 7 cm.; first phalanx, 3.5 cm.; second phalanx, 2.5 cm.; third phalanx, 2 cm.

Third finger (right) metacarpal, 7 cm.; first phalanx, 4 cm.; second phalanx, 2.5 cm.; third phalanx, 1.5 cm.; (left) metacarpal, 7 cm.; first phalanx, 4 cm.; second phalanx, 2 cm.; third phalanx, 1.5 cm.

Fourth finger (right) metacarpal, 6 cm.; first phalanx, 3 cm.; second phalanx, 1.5 cm.; third phalanx, 1.5 cm.; (left) metacarpal, 6 cm.; first phalanx, 2.5 cm.; second phalanx, 1.75 cm.; third phalanx, 1.5 cm.

Pelvis:

Circumference over crest of ilia, 56 cm.
Circumference over great trochanters, 58 cm.

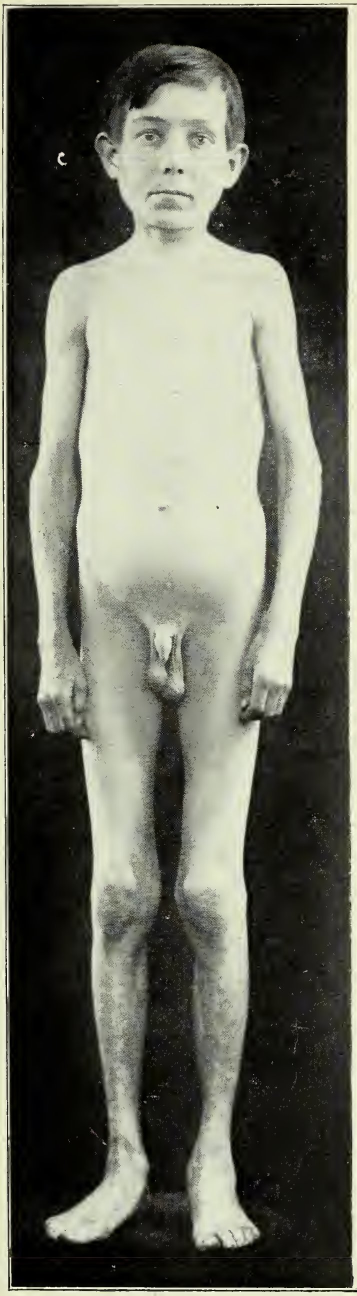

Fig. 1.—Patient affected with hookworm infantilism, front view.

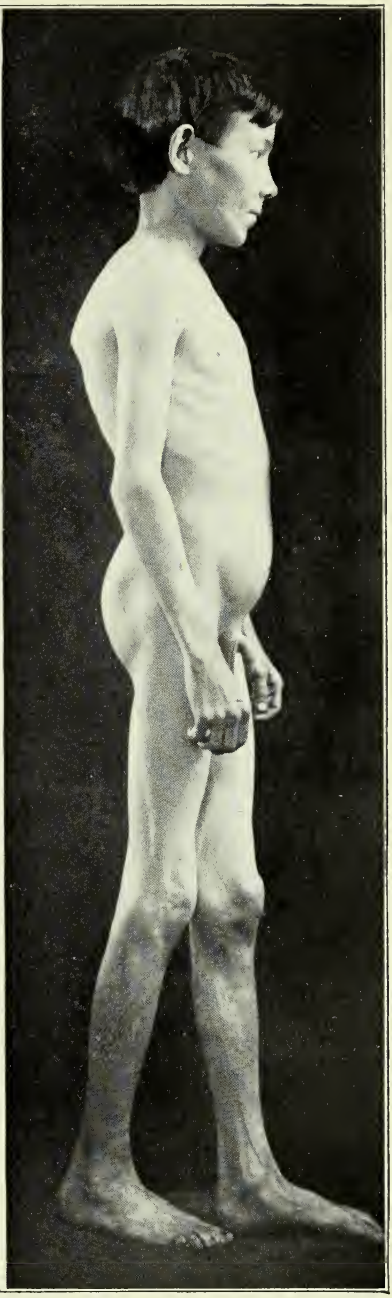

Fig. 2.—Same patient as in Figure 1, side view.

Lower extremities:

From anterior superior spine of ilium to internal condyle, both sides, 43.5 cm.

From anterior superior spine of ilium to external malleolus, both sides, 75.5 cm.

Length of feet, 20.5 cm.

It will be noticed that the dwarfing process is uniform. There is no disproportion between the lengths of the limbs and that of the trunk, and no undue size of the extremities or of the head.

Skiagraphs of the long bones of the thorax and of the pelvis show no deformity and no abnormality of any kind. There is no bowing of the shafts of the long bones, no thickening of their ends, no evidence of abnormal cartilage processes in the epiphyses, no thickening of the periosteum. The ribs are apparently of uniform thickness throughout. The pelvis is symmetrical and of proper size in proportion to the rest of the skeleton.

As a standard by which we may estimate the degree in which our patient's growth has been retarded, I have adopted the suggestion of Rotch[1] and have attempted to arrive at the anatomic age of the patient by comparing his skeleton with those of the average normal individual. For this purpose Rotch has used the skiagraphs of the bones of the wrist and has by a series of observations of normal wrists fixed a standard of development for each age. The skiagraph of my patient's wrist shows seven carpal bones well developed, namely, the scaphoid, semilunar, cuneiform, trapezium, trapezoid, os magnum, and unciform. In addition, the lower epiphyses of both ulna and radius are well developed. The shadow of the pisiform bone is barely to be seen. A reference to Rotch's table would place this wrist in Class K and cause us to estimate the true anatomic age of our patient as about 10 or 11 years. This is the estimate placed by Dr. Rotch, to whom the skiagraph has been submitted. We may conclude, therefore, that hookworm infection may retard the developmental changes to such an extent as to cause an individual of 22 to retain the grade of ossification of the average normal individual of 10 or 11.

The infantilism of hookworm disease has much in common with infantilism from certain other causes. On the other hand there are some forms of arrested development with which it stands in strong contrast and with which it is not likely to be confused. Such types are, for example, the achondroplastic dwarf, the mongolian idiot, the rachitic dwarf. From the achondroplastic dwarf, my patient is readily distinguished by the absence of the characteristic lack of proportion between the lengths of the extremities and that of the trunk. Besides there is no trident hand, no bowing of the long bones, no decentralization of the umbilicus, no prognathism as there usually is in achondroplasia. The genitalia share in the retardation, while in achondroplasia they correspond in size

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[1] Rotch, T. M.: Chronologic and Anatomic Age in Early Life, Jour. Am. M. Assn., 1908, li, 1197.

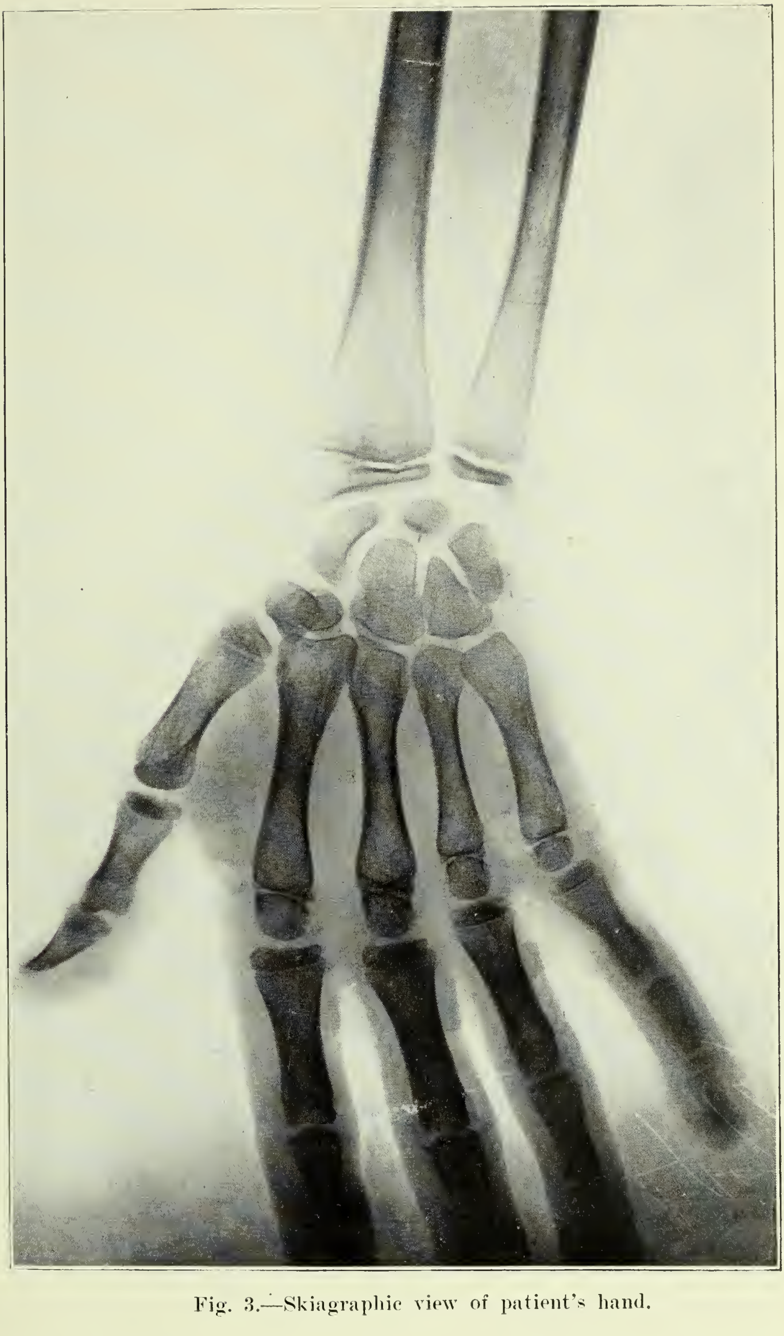

Fig. 3.—Skiagraphic view of patient's hand.

and development to the true age of the individual. The skiagraphs of the hookworm dwarf show none of the cartilage changes of the achondroplastic. The hookworm dwarf has equally as little in common with the rachitic dwarf. In rickets the bone shadow is paler than normal and the medullary canal is larger, making the cancellous tissue smaller. Hence there is a bending and bowing of the long bones. The ends of the long bones are enlarged and there is irregular cartilaginous development of the epiphyses. In addition there is an unduly large skull, squared and frequently "bossed." None of these features are present in the hookworm dwarf.

There could be no question of the difference between the hookworm infantile and the outspoken fully developed cretin. The latter, with his thick, protruding lips, big head, short thick neck, long cylindrical torso, lumbar lordosis and infantile pelvis, his thick skin and marked adiposity, as well as his drooling idiocy, presents a picture not to be confused. If the hookworm dwarf has no mental characteristics in common with the cretin, he has equally none with the mongolian idiot. In addition, he lacks the slant-eyed mongolian facies.

But there is a masked cretin, the dysthyroid or hypothyroid infantile (type Brissaud) who may have a much closer resemblance to our patient. In both there is a simple retardation of the development in general, involving not only the skeleton but the genitals and the secondary sexual characteristics; in both there may be a dry skin with dry, harsh, scanty hair. But even the masked cretin, fairly intelligent though he may be, has usually enough of the characteristics of the cretin, namely, the round full face with thick lips, small nose and thick skin, to distinguish him from the patient of the type of ours. It may not be out of place here to repeat the suggestion often made before, that infantilism of widely differing fundamental causation may be due to disturbance of the function of the thyroid and other ductless glands with internal secretion. In this sense, therefore, hookworm infantilism may be a dysthyroid condition. After all, infantilism is only a symptom-complex, not a disease. What the actual pathologic lesion is, is still to be determined for hookworm infection as for many other causative factors; it may be thyroid, pituitary, ovarian, testicular, etc., etc. The only point I wish to make here is that the masked cretin and the hookworm infantile do not differ markedly in kind, a fact suggesting a possible relation of pathology.

The cases reported by Ettore Levi[2] show that the infantilism of the type Lorain presents skeletal changes not different in kind from those in my case. The type Lorain infantile has been described as having a small

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[2] Levi, Ettore: Nouv. iconog. de la Salpêtrière, 1908, xxi, 421.

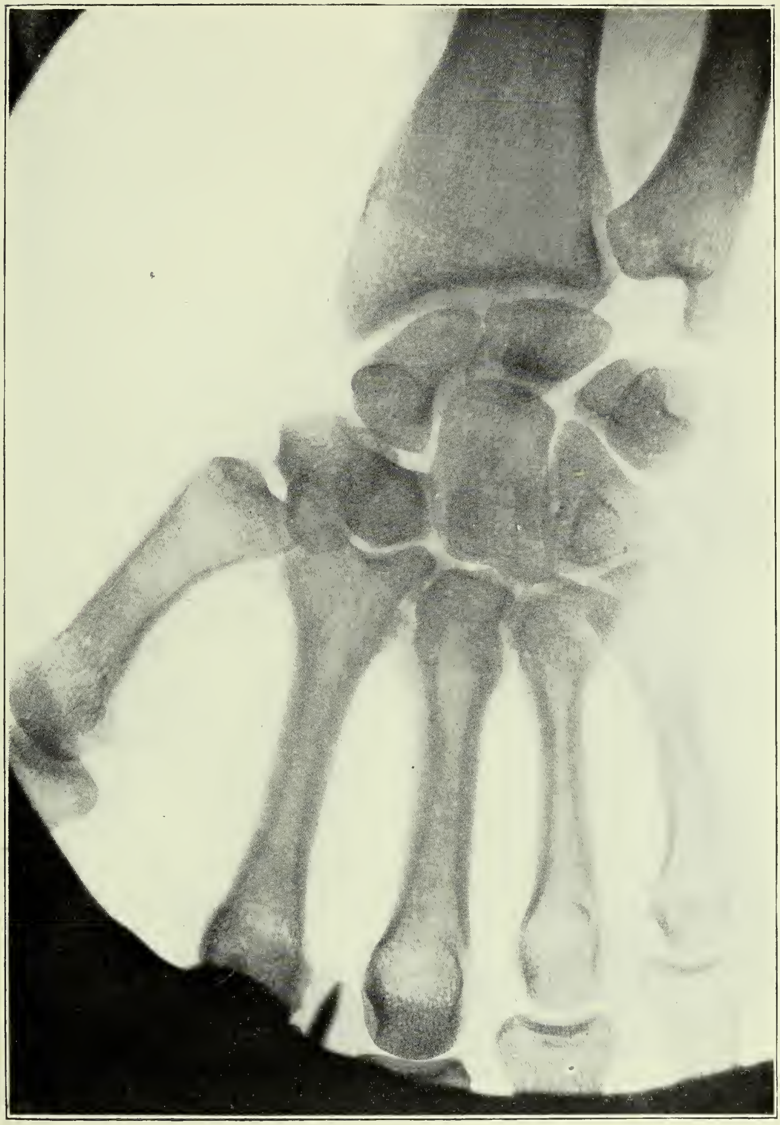

Fig. 4.—Skiagraphic view of normal adult hand for comparison.

stature, delicate, slender skeleton and form, long, slim legs, relatively small trunk, infantile sternum and pelvis, long neck with fine, pale skin. and no adipose envelop. The genitals are small and the secondary sexual characteristics are usually lacking. The dimensions of the body in general are small and the proper relation between the various parts is well preserved. An excellent example of the type is the case reported by Dr. Van Wart and myself[3] in the May number of THE ARCHIVES OF INTERNAL MEDICINE. We considered the cause of this case to be pituitary tumor, which was also a probable cause in one of Levi' cases. But infantilism of this type is also not to be considered a distinct entity from the standpoint of etiology. On the whole our hookworm infantile conforms neither to the type Brissaud (dysthyroid or athyroid) nor to the type Lorain in his general appearance, suggesting rather the second than the first and standing midway between the two. The retarded development said to be due to chronic malaria is probably analogous to that of hookworm infection and Levi speaks of Lancereaux and Ferranini's malarial cases as being of the Lorain type. Pellagra (hereditary) has also been held responsible for a similar form of infantilism.

I have found no skiagraphic study of infantilism of the type Lorain due to such causes as hereditary syphilis (unless Levi's are to be so regarded), tuberculosis (of the parents), mitral stenosis, alcohol, lead, nicotin, etc., but it seems more than probable that they would show simply a general retardation without special changes in bone or cartilage.

I conclude, therefore, that the infantilism of hookworm disease shows in general the following characteristics:

1. A general retardation of growth, symmetrical and harmonious.
2. A simple retardation of skeletal changes.
3. A failure of development of the genitals as well as the absence of secondary sexual characteristics.
4. A mental slowness and dulness (not present in my patient).
5. A general appearance which conforms neither to the Brissaud nor the Lorain type.

602 Perrin Building.

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[3] Lemann, I. I., and Van Wart, R. M.: A Case of Infantilism with Absence of Thyroid and Tumor of Pituitary, THE ARCHIVES INT. MED., 1910, v, 519.

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AMERICAN MEDICAL ASSOCIATION
FIVE HUNDRED AND THIRTY-FIVE DEARBORN AVENUE
CHICAGO

Extracted from the American Journal of the Medical Sciences, November, 1910

IPECAC IN THE TREATMENT OF INTESTINAL AMŒBIASIS.[1]

By Walter V. Brem, M.D.,
CHIEF OF THE MEDICAL CLINIC, COLON HOSPITAL,
AND
A. H. Zeiler, M.D.,
PHYSICIAN TO THE COLON HOSPITAL, CRISTOBAL, CANAL ZONE.

The temporary cessation of dysentery in amœbic infections has been an easy thing to bring about in the majority of cases, but the eradication of the infection was long our despair. The former could generally be accomplished by merely keeping the patient at rest in bed on a suitable diet; in an attempt to accomplish the latter, we treated our patients during four years with copious enemas of normal salt solution, quinine solutions in varying strengths up to 1 to 250, thymol solutions up to a strength of 1 to 500, and quinine and thymol combined in solutions of 1 to 500, and 1 to 1000, respectively. We treated many patients with intestinal amœbiasis both with and without dysentery, and some for prolonged periods of time. Among those with dysentery we never eradicated an infection and amœbæ always reappeared within a few days after treatment was discontinued, and were present when the patients left the hospital. Among the patients without dysentery we cured the infection of one with 1 to 500 quinine enemas, and of two with enemas of quinine and thymol, 1 to 500 and 1 to 1000 combined.

We have used the bismuth treatment advocated by Deeks and Shaw[2] without success, but we did not give this treatment a thorough test. However, within a short time following the presentation of the paper by Deeks and Shaw to the Medical Society of the Canal Zone, we admitted to Colon Hospital five patients with recurrences of dysentery, for which they said that they had been treated with bismuth at Ancon Hospital. These patients all had amœbæ in their stools. We cannot feel, therefore, that the conclusions of Deeks and Shaw are justified, and experience has taught us that it is very difficult in Panama to follow one's patients and to make repeated examinations of stools.

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[1] Read at a meeting of the American Society of Tropical Medicine, St. Louis, June 11, 1910.

[2] Medical Record, November 13, 1910.

IPECAC TREATMENT. On account of the recommendation of English physicians, especially Manson,[3] ipecac also was tried, but in an unenthusiastic manner. Without the salol- or keratin-coated pills the doses given were necessarily small, vomiting was frequent, and the ipecac that was retained had no effect upon the amœbæ. We were skeptical about it, as about bismuth, chiefly because of our knowledge of the pathological conditions with which we had to cope, for it was to us inconceivable that any drug given by the mouth could reach the colon in sufficient amount to be parasiticidal to amœbæ buried deep in the gut wall or protected in ulcers by a thick layer of tenacious, necrotic material. Local applications and surgical interference held out, to our minds, the greatest hope of success in the treatment of this *bête noir* of tropical and subtropical diseases.

However, after Dock's[4] communication on the subject, and after one of us had talked with him and with Boggs, of the Johns Hopkins Hospital, who also had used ipecac successfully, we determined to give the drug a thorough trial. We present our cases in detail at the end of the paper. They have been grouped according to the presence or absence of dysentery, according to the length of time that we were able to follow them, and according to the success or failure of the treatment. By "dysentery," we mean the condition manifested by abdominal pain, tenesmus, diarrhœa, and stools containing blood, pus, and mucus.

Eight cases of amœbiasis with dysentery were followed for six weeks to five and one-half months, with repeated examinations of stools for amœbæ. All were successfully treated with ipecac. Case III is the most striking and convincing case that we have had. Three cases (IX, X, and XI) of amœbiasis with dysentery were successfully treated also, but were followed less than six weeks. Three cases (XII, XIII, and XIV) of amœbiasis without dysentery were successfully treated and followed two to five months. In four cases XV, XVI, XVII, and XVIII) of amœbiasis without dysentery, the ipecac treatment failed. The four unsuccessful cases all belonged to the group of amœbic infections without dysentery; one patient was so susceptible to irritation by ipecac that he could not be thoroughly treated; three were not "bed patients," and the diet was not carefully regulated; none could be considered thoroughly treated. The amœbæ of one of these patients (Case XVI) corresponded to the description of Entamœba histolytica;[5] with Wright's stain the endoplasm took a pale blue stain, the ectoplasm a darker blue, the protoplasm was vacuolated, inclusions were present, the nucleus was ill-defined, and the chromatin scattered; in the fresh specimen the amœbæ were large, active, vacuolated, and the ectoplasm was distinct. The amœbæ of two of the patients (Cases XV and XVII) were small, sluggish, and the ectoplasm was not well defined; the endoplasm stained a deeper blue than that of Entamœba histolytica, the ectoplasm a very dark blue, the chromatin was scattered and more abundant, and the nucleus ill-defined. The amœbæ of the fourth patient (Case XVIII) seemed to be Entamœba histolytica in the fresh specimen; in the stained specimen, however, they resembled those of Cases XV and XVII, but were much larger.

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[3] Tropical Diseases.

[4] New York Med. Jour., July 10, 1909.

[5] Jour. Infec. Dis., 1908, v, No. 3.

It is quite probable that different strains of amœbæ will prove to vary in their susceptibility to ipecac. We found this to be the case, apparently, in connection with quinine. The motility of some strains of amœbæ was readily checked by a 1 to 1000 solution of quinine sulphate, and the amœbæ assumed a granular, less refractile, degenerated appearance in from twelve to fifteen minutes. On the other hand, we have experimented with a strain, the amœbæ of which, in fresh stools mixed with quinine so as to make a 1 to 250 solution, retained their motility six to nine minutes; and in 1 to 500 solutions, fifteen minutes. It seems possible, therefore, that a certain number of patients may harbor amœbæ that have the power to resist ipecac, and that a certain number of failures may be expected.

Preparation of Ipecac. Salol-coated pills were used in all the cases except one (Case VI), in which ipecac in capsules was used. Our pills were obtained from one of the reliable drug houses in the United States. The first lot of pills were covered very thinly with salol, and vomiting not infrequently followed, usually three to eight hours after ingestion of the pills. Occasionally, pills were found in the vomitus. In one instance we filtered the vomitus, which had a strong acid reaction, and immersed several of the pills in it. The salol coat was gradually dissolved, and within an hour or two the pills were disintegrated. When Simon's[6] article, in which he suggested a salol coat $\frac{1}{8}$ inch thick, appeared, we compromised and ordered pills with a salol coat $\frac{1}{16}$ inch thick. Vomiting has not occurred with these pills, but we have found that they sometimes pass through the alimentary canal before the salol coat is dissolved.[7] We must be careful, therefore, on the one hand, not to have a coat that is too thin, and, on the other hand, to have it thin enough to be readily dissolved in the intestine. The $\frac{1}{16}$ inch coat of the pills that we have used is certainly thick enough, and perhaps slightly too thick.

The Dosage and Administration of Ipecac. We have tried several systems of dosage and administration. Two patients (Cases III and IX) were given 80 grains to begin with at 9 P.M., and the dose was reduced 5 grains each night until a dose of 10 grains was reached. One patient (Case VI) was treated successfully with ipecac in capsules beginning with only 40 grains. The ipecac was preceded by an opiate. Three patients (Cases I, II, and XII) were given 120 grains during twenty-four hours, and amœbæ were never found afterward, excepting one five months later in Case XII. This is a rapid method, but we do not feel that it is a sure one. It was attempted in Case XVI, and failed, and, moreover, excited a severe dysentery. In Case VIII doses of from 40 to 80 grains were given at intervals of from two to seven days.

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[6] Jour. Amer. Med. Assoc., 1909, liii, 1526.

[7] In the discussion of the paper Simon stated that the salol coat of pills freshly prepared with fused salol was more easily dissolved than the salol coat of the pills that we used. The freshly prepared pills are probably more reliable.

We agree with those who advocate beginning with 60 grains, or, better, 80 grains, of ipecac, and reducing the dose gradually until a dose of 10 grains is reached. As a rule, it is unnecessary to continue the treatment longer, and usually advisable not to do so, for the small doses may serve only to keep up a catarrhal condition of the bowel, already excited by the large doses. Such a catarrhal condition with mild diarrhœa seems to be commonly produced.

DIET IN THE TREATMENT. Food plays an important part in the treatment The pills may be delayed in the stomach by solid food or by milk curds, until the salol coating is coroded and vomiting is excited. We have seen milk curds containing disintegrated ipecac pills vomited several hours after ingestion. One patient (Case XII) took 60 grains at night three hours after eating a light dinner, 40 grains the next morning immediately after a light breakfast of coffee and toast, and 20 grains at noon after luncheon at which some asparagus was eaten. There was no nausea or discomfort until two hours after the luncheon, when an extraordinary pulpy gelatinous mass of asparagus containing disintegrated ipecac pills was vomited. Furthermore, the residue from too much food must certainly serve to embed and scatter the ipecac so that it cannot come into thorough contact with the gut wall. While we believe that many infections may be eradicated without stringent dieting, still in all cases no solid food or milk should be given for at least six hours before the ipecac, and no food of any kind for three hours before. To insure success, the patient should be kept in bed on liquid diet, milk should not be given during the six hours preceding ipecac, and no other liquids for three hours. We make it a practice to keep the patient lying on his right side because of the possibility that gravity may help the progress of the pills into the pyloric end of the stomach. We have begun now to flush the colon with normal salt solution during the afternoon. The pills are given about 8 or 9 P.M.

SUMMARY. 1. We despaired of success after four years of experience in attempting to eradicate intestinal amœbiasis by means of rest, dieting, and lavage of the colon. We used copious enemas of normal salt solution, quinine, thymol, and quinine and thymol combined.

2. We have apparently cured 14 amœbic infections with ipecac: 8 with dysentery, followed six weeks to five and one-half months

with repeated examinations for amœbæ; 3 with dysentery, followed less than six weeks; 3 without dysentery, followed two to five months. We have failed to eradicate the infection in 4 cases, but these were not thoroughly treated.

3. The thickness of the salol coat of the ipecac pills must be carefully regulated so as to prevent vomiting on the one hand, and on the other, the passage of intact pills through the intestinal canal.

4. Probably the best dosage and method of administration is to begin with 60 or 80 grains at bedtime and decrease the dose 5 grains daily until a dose of 10 grains is reached. Rapid cures may sometimes be effected by giving 40 grains three times during twenty-four hours.

4. The patient should be at rest in bed and on liquid diet; no solid food or milk should be given for at least six hours previous to the ipecac, and no liquids for three hours previous. No opiate is necessary.

5. Our experience indicates that a large proportion of amœbic infections can be eradicated by ipecac treatment. It is far superior to any treatment that we have hitherto tested, and it should always be given a thorough trial before surgical treatment is attempted.

REPORT OF CASES.

A. CASES OF INTESTINAL AMŒBIASIS WITH DYSENTERY TREATED SUCCESSFULLY WITH IPECAC AND FOLLOWED SIX WEEKS TO FIVE AND ONE-HALF MONTHS AFTERWARD.

CASE I.—No. 20725, white, American; on the Isthmus six months; admitted November 2, 1909.

History. Dysentery in the Philippines in 1909, lasting six weeks, on account of which the patient was sent home. He recovered and did not have dysentery again until he came to the Isthmus. About one month ago he began to have diarrhœa, tenesmus, and bloody stools, for which he received bismuth treatment at Ancon Hospital. On admission to Colon Hospital, the patient had estivo-autumnal malarial fever, diarrhœa, tenesmus, and bloody stools. Microscopic examination of the stools showed large, active amœbæ. Copious enemas of normal salt solution were given twice daily for thirteen days, and then enemas of 1 to 1000 quinine solution twice daily for thirteen days. At the end of this time, November 27, amœbæ were still present in the stool, though the dysentery had ceased.

Treatment. On November 29 the patient was given 120 grains of ipecac in three doses of 40 grains each, morning, noon, and night.

Subsequent History. The treatment was followed by a recurrence of malarial fever, November 30, and by a sharp attack of diarrhœa with bloody stools lasting about one week. There was no further intestinal trouble, however. The patient was last seen in May, 1910, more than five months after treatment.

Stool Examination. During the dysenteric attack following ipecac the stools were negative for amœbæ, and none were found on subsequent examinations. Examinations were made December 3 and 13, 1909, January 29, February 7, 12, 17, and 20, March 26, April 7, April 13, 1910.

Case II.—No. 20994, white, American; on the Isthmus eighteen months; admitted November 17, 1909.

History. Dysentery about eleven months before admission; treated at Santo Tomas Hospital, in Panama, for six or seven weeks; was better for one week, but then the dysentery recurred. Three weeks after discharge from Santo Tomas (eight or nine months before present admission), he entered Ancon Hospital and received bismuth treatment for six weeks. Dysentery has persisted intermittently since discharge from Ancon. Entered Colon Hospital first on September 16, 1909; the diagnosis made was amœbic dysentery; amœbæ were present in the stools; treated until November 14 (nearly two months) with enemas twice daily of normal salt solution, alternating with enemas twice daily of 1 to 1000 quinine solution. Dysentery improved, but amœbæ were still present on discharge. Three days after discharge the patient was readmitted (present admission) to Colon Hospital with dysentery associated with large, active amœbæ.

Treatment. Ipecac in 5 grain salol-coated pills, 120 grains in three doses of 40 grains each, was given November 4, 1909.

Subsequent History. The patient vomited one hour and three hours after the first dose, and three pills were ejected. No further vomiting. A slight diarrhœa for one day followed the ipecac, and then the stools became formed and movements normal.

Stool Examination. The patient was under observation until May, 1910 (five months), and there was no recurrence of dysentery. All stool examinations made after the ipecac treatment were negative for amœbæ. Examinations were made November 26, December 10, 12, 1909, March 22, April 17, April 29, 1910.

Case III.—No. 21743, white, American; on the Isthmus three and one-half years; admitted January 8, 1910.

History. Dysentery three years ago with abscess of liver; operated on at Ancon Hospital with good recovery. Four attacks of dysentery since: (1) February, 1909, in Ancon Hospital, eight days, treated with bismuth; no irrigations (2) June, 1909, Colon Hospital, nineteen days, amœbæ found, no diarrhœa, but severe burning sensation in lower abdomen; treated with copious enemas of normal salt solution twice daily; improved; (3) July, 1909, Colon Hospital four months, slight diarrhœa on admission, intense continuous burning sensation in lower abdomen, numerous amœbæ in stools;

appendicostomy, July 19; cecum and ascending colon were found to be enormously thickened, purple in color, extensively diseased; irrigations through appendix twice daily for eight weeks with 1 to 4000 and 1 to 3000 quinine solution, then no irrigations for about eight weeks; improvement; (4) January, 1910 (present admission), two months after last discharge, nine to thirty movements daily, tenesmus, blood, mucus, intense pain.

Stool Examination. Mucus, blood, pus, enormous numbers of large, active amœbæ, distinct ectoplasm, vacuolated; many with red blood-corpuscles engulfed; stain with Wright's stain like amœbæ of "Cochin China Dysentery;"[8] that is, they take a darker blue than Entamœba histolytica, and contain an enormous quantity of chromatin diffusely scattered; no discernible nucleus.

Treatment. Ipecac, 80 grains at 9 P.M., January 9. The dose was decreased 5 grains each night until reduced to 5 grains January 24. Patient vomited twice, six and seven hours after the first dose and twice, four and ten hours after the third dose. The patient was discharged February 6, about one month after admission.

Subsequent History. While in the hospital the number of stools per day decreased to two or three; they were semisolid and contained mucus. By February 20 the stools had become normal. Patient was under observation four and one-half months after treatment.

Examinations for amœbæ were as follows:

January 10. Ipecac begun January 9. Amœbæ found in only one of seven preparations examined.

January 11. A few amœbæ found without difficulty.

January 12. Three preparations examined, many amœba-like bodies found, but no motile ones seen.

January 14. One motile amœba found in searching four preparations.

January 15. Negative for amœbæ.

January 16. Negative for amœbæ.

January 17. Negative for amœbæ.

January 27. Negative for amœbæ.

January 28. Negative for amœbæ.

February 2. Negative for amœbæ.

February 5. Negative for amœbæ.

February 13. Patient returned for examination (discharged one week ago). He has had four or five movements daily, semisolid stools with mucus, but no blood, pain, or tenesmus. Stool examination: Semisolid, masses of mucus, no blood or pus, no amœbæ. (Four preparations examined.)

February 20. One or two normal formed movements daily, no mucus, no pain. Stool examination: Negative for amœbæ, blood, pus, or mucus.

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[8] Annales de l'institute Pasteur, March, 1909, t. xxiii, No. 3.

March 20. Stools formed, normal, one daily. Two stools examined, both negative.

April 24. Stools formed, normal; two preparations negative for amœbæ, blood, pus, mucus.

May 29. Patient in excellent condition, bowels regular, stools normal. No stool obtained for examination.

Case IV.—No. 21362, colored, Colombian; on the Isthmus three days; admitted December 13, 1909.

History. Dysentery began two months ago; diarrhœa, blood, abdominal pain. During first week in hospital patient had three to five movements a day, some tenesmus, mucus, and blood. Large active amœbæ were found.

Treatment. Ipecac, 40 grains December 15, in one dose; 35 grains December 16; 30 grains December 17; 25 grains December 18.

Subsequent History. No nausea or discomfort after ipecac. One stool a day after December 20. Discharged December 29; has been under observation five and one-half months. No further intestinal trouble.

Stool Examinations. January 3, 1910, large amœba-like bodies, no motility.

February 1. Negative for amœbæ.

March 18. Negative for amœbæ.

April 20. Negative for amœbæ.

May 30. Negative for amœbæ.

Case V.—No. 21487, white, American; admitted from U. S. S. Prairie, December 23, 1910.

History. Dysentery three years ago in Guam, L. I. Was in hospital fifty-four days; severe attacks of diarrhœa at intervals since then; last attack seven months ago. Present attack began three days ago, severe diarrhœa, fifteen or sixteen movements a day, griping and tenesmus, no blood. On admission patient had diarrhœa, two to nine movements a day. Microscopic examination showed blood and pus; no amœbæ were found in first three examinations; the fourth examination revealed large active amœbæ.

Treatment. Copious enemas of normal salt solution twice daily for two weeks, then discontinued, and rest and dietetic treatment given for about two weeks. Treatment with ipecac was begun January 24, 9 p.m., 80 grains; January 25, 75 grains; January 26, 70 grains; January 27, 65 grains; January 28, 60 grains.

Subsequent History. Ipecac treatment was followed by diarrhœa, with six to thirteen movements daily for one week, then two to five movements for another week. No blood, some mucus. After the second week there were from one to three or four movements daily; stools were semiformed and at times contained mucus.

Patient was under observation until March 19, 1910, about eight weeks after ipecac treatment was begun.

Stool Examinations. All negative for amœbæ, January 25, February 2, 5, 8, 18, 20, 21, March 4, 8, 1910.

Case VI.—No. 21644, colored, Jamaican; on the Isthmus five years; admitted December 31, 1909.

History. Sick three months with disentery. On admission patient was having from four to eight movements per day, with tenesmus, blood, and mucus. Microscopic examination showed large, active amœbæ, having the staining characteristics described by Craig[9] for Entamœba histolytica.

Treatment. Treatment with ipecac in capsules was begun December 31, 1910. The three initial doses were 40 grains given at 8 P.M. on succeeding days, then 30 grains daily for two days, 20 grains daily for two days, 10 grains daily for eleven days. The ipecac was preceded by an opiate.

Subsequent History. No vomiting after ipecac; a mild diarrhœa persisted during the ipecac treatment. After treatment was begun the patient was under observation a little over six weeks.

Stool Examinations. All negative for amœbæ, January 11, 13, 24, 25, February 13, 16, 1910.

Case VII.—No. 21857, colored, Jamaican; admitted January 17, 1910; on the Isthmus four years.

History. Exploratory laparotomy on previous admission and a peculiar condition of the liver found, thought to be gummatous. Patient admitted this time with œdema of the feet and legs and ascites. He had had pain in his bowels for three weeks with diarrhœa, passing blood and mucus. Two examinations of stools, January 18 and 22, were negative for amœbæ, but positive for blood and pus. The patient was having from three to five movements a day. On February 18, innumerable large, active amœbæ were found; these were vacuolated with well-defined ectoplasm and stained like Entamœba histolytica with Wright's stain.

Treatment. Ipecac, 40 grains February 19, 20, and 22; 35, 30, and 25 grains February 23, 24, and 25.

Subsequent History. No nausea or vomiting and no increase of diarrhœa during treatment. Diarrhœa reduced from four to six movements daily before, to one to three after treatment. Patient was under observation for nearly two months after ipecac was given.

Stool Examinations. Negative for amœbæ, February 18, March 17 and 25, April 10, 1910.

Case VIII. No. 22,005, white, Italian; on the Isthmus twenty-seven months; admitted January 26, 1910.

History. Diarrhœa for two weeks with as many as twenty movements a day, great weakness, distress after eating for one year. Hemorrhoids. Examination of stools showed mucus, blood, and innumerable amœbæ, large, active, vacuolated, with well-defined ectoplasm. They stained unlike either Entamœba histolytica or Entamœba coli[10] or the amœbæ of Cochin China dysentery. The amœbæ, on account of their size and their stain affinities, gave one an impression of solidity: they seemed massive. The endoplasm took almost a red stain because of the enormous quantity of chromatin, and the ectoplasm was almost a blue black; the nucleus was well-defined and rich in chromatin (Wright stain).

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[9] Loc. cit.

Treatment. Ipecac, 80 grains on January 27; 40 grains, January 28 and 30, February 6, 11, and 14.

Subsequent History. Vomited several times three to six hours after taking ipecac; had no diarrhœa. Was transferred to the surgical side and operated on for hemorrhoids February 21. Readmitted March 20, 1910, for another operation on an old ventral hernia. Under observation over two months and had no further dysenteric trouble.

Stool Examinations. January 28, amœbæ present. Examinations negative for amœbæ, January 30, February 9, 16, 17, 18, 20 and 21, March 21.

B. INTESTINAL AMŒBIASIS WITH DYSENTERY TREATED SUCCESSFULLY WITH IPECAC AND FOLLOWED LESS THAN SIX WEEKS.

CASE IX.—No. 21345, white, Scotchman; has lived in Nicaragua; on the Isthmus one day; admitted December 12, 1909.

History. Dysentery two and one-half years ago, with several recurrences of active dysentery since, and diarrhœal attacks nearly every month. He was treated in Ancon Hospital during one dysenteric attack, was in bed thirteen days, and received large doses of bismuth. He has been in England for eighteen months, and while in Liverpool had dysentery and was treated in a hospital there. The present attack began one week ago on shipboard *en route* from England to Colon. He has been having intense abdominal pain, tenesmus, and diarrhœa, and stools have contained mucus and blood. On admission, the patient was having four to nine movements daily, pain was intense and required morphine, the stools were thin, contained blood, and numerous small mucous masses, which were composed almost entirely of amœbæ closely packed together in the field of the microscope. These amœbæ were large, active, vacuolated, had a well-defined ectoplasm, and contained numerous red blood corpuscles; fourteen corpuscles were included in one amœba. They stained with Wright's stain like amœbæ of Cochin China dysentery. Numerous amœbæ were found December 12, 14, 15, and 17.

Treatment. Ipecac was begun December 18, 8 P.M., 60 grains; December 19, 80 grains; December 20, 60 grains; dose decreased 10 grains each night until a dose of 10 grains was reached.

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[10] Craig, loc. cit.

Subsequent History. Patient vomited a few times six or eight hours after taking the ipecac. The stools decreased in number during the treatment; before discharge, January 8, 1910, only one formed normal stool was passed daily. The patient left January 8, 1910, for Nicaragua, and has not been heard from. He was under observation nineteen days after the first negative stool examination.

Stool Examinations. Two amœbæ found December 20 in five preparations. Stools negative for amœbæ, December 22, 23, 24, 30, 1909, and January 2, 3, 5, 8, 1910.

Case X.—No. 21356, colored, Bolivian; on the Isthmus two years; admitted December 13, 1909.

History. Sick three months with dysentery. On admission, four to ten movements daily; stools contained mucus and blood and innumerable large, active amœbæ, vacuolated with well-defined ectoplasm and staining with Wright's stain like Entamœba histolytica.

Treatment. Ipecac was begun December 15, 8 a.m., 40 grains; dose decreased 5 grains a day for three days; only four doses given.

Subsequent History. No vomiting; diarrhœa persisted, but stools decreased in number while ipecac was being given; stools then became normal for two weeks; then there was a mild diarrhœa for ten days after patient was given "full diet." He was discharged January 17, 1910, in good condition, with normal stools, one month after ipecac treatment was begun.

Stool Examinations. Negative for amœbæ, December 18, 22, 25, 1909, January 1 and 8, 1910.

Case XI.—No. 23304, white, American; on the Isthmus five years; admitted April 17, 1910.

History. Onset three days ago with diarrhœa; passed blood two days ago. Never had dysentery before. On admission patient had five to twelve movements daily, with pain and tenesmus; stools contained blood and numerous active amœbæ.

Treatment. Ipecac, April 18, 9 p.m., 60 grains; April 20, 40 grains; April 21, 30 grains; April 23, 20 grains.

Subsequent History. No discomfort from treatment, two to four movements daily when discharged April 27, 1910. Patient was seen May 21, and he was in good condition, and had had no recurrence of intestinal trouble. He was under observation one month after ipecac treatment was begun, but the stool examinations covered only eight days.

Stool Examinations. April 19, a few amœbæ, blood, and pus.

April 20. No amœbæ or blood, some mucus.

April 22. Stool semisolid, negative for amœbæ, blood, and mucus.

April 24. Stool negative for amœbæ, normal.

April 27. Stool negative for amœbæ, normal.

C. CASES OF INTESTINAL AMŒBIASIS WITHOUT DYSENTERY TREATED SUCCESSFULLY WITH IPECAC AND FOLLOWED FOR SIX WEEKS TO FIVE MONTHS.

CASE XII.—White, American; on the Isthmus four years.

History. The patient had been under observation two years, had never had dysentery, but had had occasional mild attacks of diarrhœa, and bowels showed a tendency toward looseness, two to four semisolid movements daily. There had never been blood in the stools, but some mucus, and the patient was frequently troubled with flatulency. Many examinations of stools during two years had always shown the presence of numerous large, active, vacuolated amœbæ with well-defined ectoplasm. They stained with Wright's stain like Entamœba histolytica. Rest and dietetic treatment and enemas of normal salt solution, quinine and thymol had no effect upon the amœbæ. They averaged fifteen to twenty per field (B and L, 1 ocular, $\frac{2}{3}$ objective) of the microscope a few days before treatment with ipecac.

Treatment. January 2, 1910, Ipecac, 60 grains, 9 P.M.; January 3, 40 grains, 8 A.M., and 20 grains, 1 P.M.—120 grains during twenty-four hours.

Subsequent History. Patient vomited two hours after the last dose of ipecac, and two or three pills were ejected. The treatment was followed by diarrhœa for two days. There was some tendency toward flatulency and mild diarrhœa for several weeks, but there has been no trouble now for three months. The patient has been under observation for five months since the treatment.

Stool Examinations. Negative, January 4, 10, 18, February 2, 13, April 25. On May 27, after a prolonged search, one amœba was found. This amœba was twelve microns in diameter, was very sluggishly motile, no ectoplasm could be seen, no vacuoles and no engulfed bacteria could be made out. It appeared to be Entamœba coli, and was not, we believe, a relic of the former infection. Only one was found.

CASE XIII.—No. 21322, white, American; on the Isthmus twenty months; admitted December 10, 1909.

History. Pain in lower abdomen for two weeks; has been having alternating attacks of diarrhœa and constipation; never passed blood. No diarrhœa or constipation in the hospital. Stool examination showed small amœbæ which could not be definitely classified, no blood.

Treatment. December 21, ipecac in 5 grain salol-coated pills, 80 grains at 8 P.M.

Subsequent History. Stool examinations December 22 and 23, negative for amœbæ. Patient was discharged December 24, but returned for examination January 3, 1910, when numerous amœbæ were found. On January 9, amœbæ were still present, and patient was advised to return to the hospital for more thorough treatment. He did so on January 10 (No. 21755).

Second Treatment. Ipecac was begun January 10, an initial dose of 80 grains being given at 9 P.M. This dose was decreased 5 grains each night for one week until a dose of 50 grains was reached, when the treatment was discontinued.

Subsequent History. Vomiting occurred once, and a mild diarrhœa persisted during the treatment, but quickly cleared up afterward. The patient was last seen May 30, 1910, about four and one-half months after the treatment. He was in excellent health and stools were normal.

Stool Examinations. Negative for amœbæ, January 11, 12, 13, 15, 16, 17, 18, February 6 and 22, April 3, May 30.

CASE XIV.—No. 21529, white, American, on the Isthmus three and one-half months; admitted December 27, 1909.

History. Diarrhœa more or less continuously for nineteen years; at times passed blood; no tenesmus for ten years; has been unable for ten years to void urine without having a bowel movement. Mild diarrhœa in the hospital, no hœmorrhoids, no abdominal tenderness, no tenesmus, no blood in stools, but numerous large, active amœbæ, about five per field (B and L, 1 ocular, $\frac{2}{3}$ objective) of the microscope.

Treatment. Ipecac was begun December 29, 80 grains at 9 P.M. The dose was reduced 5 grains each night subsequently until a dose of 10 grains was reached.

Subsequent History. No nausea or vomiting was caused by ipecac; diarrhœa was increased during the treatment to five or six movements, but subsided when ipecac was discontinued. Patient was discharged January 17, 1910; he was then having one or two movements daily. He was seen last February 27, 1910, and up until that time he had been having three or four stools daily, semiformed, normal color, no mucus or blood, no tenesmus. He was under observation nearly two months after ipecac treatment was begun.

Stool Examinations. Negative for amœbæ, January 3, 5, 6, 7, 14, 30, February 13 and 27, 1910.

D. INTESTINAL AMŒBIASIS WITHOUT DYSENTERY TREATED UNSUCCESSFULLY WITH IPECAC.

CASE XV.—No. 21336, white, Frenchman; on the Isthmus six years; admitted December 11, 1909.

History. Amœbic dysentery and liver abscess in 1907; operated on at Ancon Hospital with good recovery. No recurrence of dysentery. Stools showed a moderate number of small sluggish amœbæ (7 to 14 microns); ectoplasm fairly well defined; small vacuoles, greenish refractility, no red blood cells engulfed. They stained with Wright's stain a rather dark blue for Entamœba histolytica; the ectoplasm stained more deeply than the endoplasm, the nucleus was ill-defined, and the chromatin scattered.

Treatment. Ipecac in 5 grain salol-coated pills begun December 22, 9 P.M., 80 grains; December 23, 70 grains; December 24, 65 grains; December 26, 60 grains; December 27, 55 grains; December 28, 50 grains.

Subsequent History. The patient vomited several times six to eight hours after taking ipecac and had a mild diarrhœa, which quickly subsided. A second course of ipecac treatment was given, but the patient did not return for examination.

Stool Examination. December 29, 1909, negative for amœbæ. January 2, 1910, negative for amœbæ. January 9, 1910, a few small amœbæ like the ones described above.

CASE XVI.—No. 22721, white, American; on the Isthmus five years; admitted March 14, 1910.

History. Constipation six months, burning sensation in abdomen one month. Loss of weight; no diarrhœa. Stools contained numerous large, active amœbæ that stain like Entamœba histolytica.

Treatment. Ipecac, March 15, 60 grains; March 16, 40 grains.

Subsequent History. Ipecac treatment excited a severe dysentery, and had to be discontinued. Patient discharged March 23, 1910.

Stool Examinations. Negative for amœbæ, March 17, 20, and 23. On April 15, numerous large, active amœbæ were present.

Second Treatment. The patient took three doses of ipecac, 50 grains, on successive nights before readmission to the hospital. A dysentery was excited again, and the amœbæ persisted.

Second Admission. May 9, 1910. Patient returned to the hospital and is still under treatment. Each attempt to give large doses of ipecac excites a dysentery, and not more than twenty grains can be given. The failure of the ipecac treatment in this case seems to be due rather to the idiosyncrasy of the patient than to the ineffectualness of the treatment.[11]

CASE XVII.—No. 23586, white, American; on the Isthmus five years; admitted May 3, 1910.

History. Amœbic dysentery in Ancon Hospital in 1907, active dysentery for three months. Mild attack of dysentery in 1908, duration ten days. Treated both times with quinine and thymol irrigations; has been feeling weak, with malaise and indigestion, two months. Tendency to constipation. No diarrhœa. Before admission, patient's stools were examined, and small sluggish amœbæ were found resembling those in Case XV. Ipecac was given, beginning with 40 grains and decreasing 5 grains daily until doses of 10 grains were reached. There was no disturbance from the treatment. The patient then returned for examination and the same kind of amœbæ were still present. He then entered the hospital.

Treatment. Ipecac, May 4, 80 grains; May 6, 60 grains; May 8, 9, and 10, 50 grains each day.

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[11] Recovery subsequently followed the use of 20 grains of ipecac daily for a prolonged period.

Subsequent History. Some abdominal discomfort and diarrhœa during treatment. The pills were a new lot, with a thicker salol coat, and a few, at least, passed through the alimentary canal without dissolving and were found in the feces. The patient was discharged May 15, 1910.

Stool Examinations. May 7, amœbæ, mucus, stool formed.

May 8. Amœbæ, stool semisolid.

May 9. Amœbæ, stool semisolid.

May 10, 11, 12, and 15. Negative for amœbæ.

May 22. Patient returned for examination. He has been constipated since discharged, has small, hard stools, feels very badly, weak, and easily fatigued, sweats profusely. Stools formed, no blood or mucus, numerous small amœbæ like those found on previous examinations and in Case XV. The patient promises to return for treatment.

Case XVIII.—No. 23918, white, American; on Isthmus ten months; admitted May 20, 1910.

History. Never had dysentery; present illness began four days ago with diarrhœa. Patient had no diarrhœa in the hospital, and stools were normal in appearance. Microscopically there was no blood or pus, but very numerous large, active, vacuolated amœbæ with well-defined ectoplasm. With Wright's stain the endoplasm took a good blue, darker than the pale blue of Entamœba histolytica, the ectoplasm was deep blue, the nucleus ill-defined, and the chromatin abundant and scattered They resembled more closely the amœbæ of Cochin China dysentery.

Treatment. Ipecac in 5-grain salol-coated pills, May 22, 60 grains; May 24, 50 grains; dose decreased five grains daily for five days until a dose of 25 grains was reached. The patient was allowed "full diet" during the treatment.

Subsequent History. Patient vomited once during treatment; no diarrhœa; discharged May 30, 1910.

Stool Examinations. May 28, negative for amœbæ.

May 30. Numerous amœbæ like those described above.

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WHAT IS HEAT EXHAUSTION?*

By P. A. Surgeon, W. H. RENNIE,
U. S. Navy.

Gentlemen: All attacks of heat resolve themselves into three classes.

Sunstroke, caused by the actinic rays of the sun in the physically enfeebled. During the hot season one already fatigued, and perhaps with arteries sclerosed, experiences a sudden collapse, or a more gradual inset, with flushed face, headache, rise of temperature, quick, full pulse, syncope and paralysis of heart and respiration as is found in cases of shock. Death may be almost immediate; or develop a train of symptoms of persistently recurring headaches, mental irritability, hypersensitiveness to heat, light and sound, delirium, restlessness and sleeplessness, nausea, loss of memory, intellectual impairment, tremor, convulsions, etc.

Of the second class, Siriasis, Manson says: "It is well known that neither high atmospheric temperature per se, nor high bodily temperature, unless the latter be associated with some special toxins, give rise to symptoms at all like those of Siriasis. Considering these two facts, and at the same time the peculiar and capricious distribution of the disease, the circumstances that its prevalence curve does not always correspond with the atmospheric temperature curve; that the degree of prevalence varies in the endemic area from year to year; that it is not most prevalent in the hottest years, seasons, or places; that it becomes epidemic at times; that it runs a definite course; that it may relapse; that in many instances it has definite premonitory symptoms; that it has peculiar lesions and that it tends to terminate by crisis; in other words, that it behaves like pneumonia or any other specific fever. Sambon has boldly asserted that Siriasis is a germ disease, like Yellow Fever or Dengue, and like these is caused by some organism which demands for its development a high atmospheric temperature and certain, as yet unknown, local conditions."

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*Read at the Seventh Annual Meeting of the American Society of Tropical Medicine, St. Louis, Mo., 1910.

The third class of cases, of greatest interest and importanec to the medical officers of the U. S. Navy, never occurs except in the presence of high artificial temperature in confined quarters and without proper ventilation, but are we justified in assuming great heat to be the essential cause, rather than a necessarily concomitant one? Is heat alone sufficient to produce the train of symptoms whose complex is recognized as Heat Exhaustion? It is of daily observation that many men expose themselves to this exciting cause without the appearance of any suspicion of trouble whatever, yet many a man, as in seasickness, will resist such attacks for years only to succumb at last.

This is absolute proof that heat alone will not succeed in so overtaking a man in health. Let me describe a case of ordinary severity:

A man in apparent health at work in the fireroom for a longer or shorter period of time, and at any minute of his four-hour watch, is suddenly, for the most part, overcome with weakness, cold, clammy skin, staggering blindness, and falls prostrate, with or without cramps; his shipmates remove him from the heat, transporting him to the sick bay, where he receives stimulation and applications of heat; his pulse is weak and rapid, and in fact is a picture of the classic collapse. In a few hours, 24 hours at the most, he has recovered and, in all likelihood, returned to his work in the fireroom below. Was this man unknowingly below par that he could not withstand the customary exposure to the same degree of heat? Certainly muscular fatigue cannot be asserted as the cause, because it may occur in the beginning of a watch. Intemperance, likewise, has been assigned as the forerunner, then how explain the attacks in men some days at sea, or in men of known habits of sobriety? Oft times some disturbance of the stomach or intestinal tract has been suspected, yet we have cases where no such trace has, at least, been discoverable.

Medical Inspector Oliver Diehl, U. S. Navy, reports in the U. S. Naval Medical Bulletin for April, 1910, the case of a man becoming unconscious for a few minutes with free perspiration, dilated pupils, pulse soft and accelerated, no convulsions or cramps; the temperature of the fireroom was 115° F; the man returned to duty the following day. Also another similar case, with an added oppression and pain in the anterior chest. No cause is here assigned; the temperature of the fireroom was only 115° F.

In the annual report of the Surgeon General, U. S. Navy, for 1909, P. A. Surgeon G. H. Hathaway, U. S. Navy, says: "During the standardization runs of the U. S. S. Cheyenne at maximum speed the temperature in the fireroom rose to 140° F., which is about 10° higher than under previous similar conditions when burning coal. Nevertheless in the higher temperature no case of heat prostration occurred, nor during the cruise has any member of the engineer's force succumbed to the heat. It is thought that the slight amount of physical exertion required to regulate the burners, as compared to passing coal, enables the fireroom watch to withstand a greater elevation of temperature. While cruising the fireroom force is reduced to about one-half those for coal fuel, which is of some sanitary advantage." This case would infer muscular fatigue and crowding as conducive to attacks.

In the April, 1910, number of the U. S. Naval Medical Bulletin, Surgeon J. T. Kennedy, U. S. Navy, speaking of heat cases on board the U. S. S. Colorado, says: "There had been no sickness or prolonged cruising to depress vitality; temperature only 120, modified by force draft and a low relative humidity, so that heat exhaustion, like seasickness, would seem to be the expression of a body seeking to adjust itself to an environment, the symptoms resulting from the temporary lack of adjustment. Since that time no cases have appeared, although the ship has sailed under worse conditions of heat and oppression, coaling has gone on under burning skies, and fatigue and depression incident to hard work and little play has been the rule." Thus sustaining just the contrary opinion of the former case.

Assistant Surgeon M. E. Higgins, U. S. Navy, in the April number of the Naval Medical Bulletin, 1910, quotes a case in a man 38 years of age, in excellent health during his 18 years in the fireroom: "He has a moderate arteriosclerosis with thickened radicals and high tension pulse, having used alcohol for years and frequently to excess. On the day of his attack the temperature of the fireroom was 130° F. About 2 p. m. he was brought to the sick bay suffering with severe muscular cramps, involving especially the abdominal muscles and the flexers of the extremities. The cramps were tonic spasms lasting for several minutes. Any change of position or voluntary movement was sufficient to precipitate a spasm of one or more muscle groups, the pain in the affected muscles was agonizing in character. When first seen the man was sweating profusely, and he continued to sweat for several hours. I have never seen a more violent or prolonged perspiration. The pulse was 130, of high tension; temperature 98° F., respiration 20. The tongue was dry and heavily coated. There were no cerebral symptoms. In six hours the cramps had entirely ceased, and with the exception of a sense of soreness in the affected muscles, which persisted for several days, the patient was comfortable. No urine was passed until the following morning, when he voided 250 c. c., Sp. gr. 1020 and high color. Heller's test gave a thick ring of albumin, and there were many finely granular casts. On the second day there appeared but a trace of albumin and a few casts. Five days later neither casts nor albumin were present and subsequent examinations have shown the same result. As Dr. Higgins remarks, the presence of albumin and casts in the urine, and free perspiration are not the rule. This man was an alcoholic for years and of long service in the fireroom.

During the cruise of the battleship fleet around the world, not a few cases occurred. Sixteen of these were studied by Surgeon A. G. Grunwell, U. S. Navy, on board the U. S. S. Kentucky; in his report we find the attacks occurred in July in tropical waters, and because of rough weather, the confined air was vitiated by the closing of the hatches. In most cases he found some disturbance of the gastro-intestinal tract (toxaemia), and advances the belief that "we need look no further than the tetanus bacillus for the production of the poison" which is absorbed from the intestinal tract.

The gravest and most interesting case, which by the way did not happen in the fireroom, was that of a private marine while coaling ship in Manila, P. I., about 6:30 in the morning. "A large, powerful and apparently healthy may of 22 years, was suddenly stricken, while wheeling coal on deck, with vertigo and violent headache. He was carried up on the bridge in the open air, and when he was seen a few minutes later convulsive twitchings had commenced. These increased rapidly in severity, becoming general tonic spasms and were in all respects so similar to the spasms of tetanus that, except for the etiology and the absence of wounds or the history of any, a diagnosis of that disease would have been made without hesitation. When fully established, the spasms seemed always to begin in the face, spreading in regular order to the neck and chest, then becoming general. Often this succession would occur with great rapidity, though sometimes risus sardonicus, and the occurrence of intermittent spasmodic contractures of the pectorals and diaphram would give warning of the approach of a general tetanic seizure. As improvement set in the spasms also abated in regular order, risus and the twitching of the pectorals being the last to disappear. During the height of the seizures, the spasms were very painful, and a marked tendency to opisthotonos was shown. There was, also, double convergent squint, the pupils being evenly, moderately contracted. Headache was excruciating and consciousness was never lost, though he became decidedly somnolent at times, probably from the effects of the morphine and chloroform administered to control spasms. Throughout the pulse was full, strong and regular, ranging from 60 to 74 beats per minute, and the temperature never rose above 100° F, either by axilla or mouth. Once only did vomiting occur, and then in the evening, after the administration of a small quantity of water, in spite of the fact that small quantities of not very cold water had been given from time to time during the day and retained. The tongue was slightly coated. It was very noticeable that currents of air, a touch, sudden noises, etc., were liable to, and usually did, produce a spasm, as in tetanus. The convulsions were readily controlled by a few inhalations of chloroform, after the administration of morphine. During the afternoon, the convulsions gradually subsiding, the patient passed a comparatively quiet night, without spasms and with considerable sleep. The next morning he complained of pain in his jaws, which were a little swollen and of toothache and headache. He was left in the open air during the night, but with the morning a steady rain set in necessitating his removal below to the sick bay where it was close and hot. Shortly after his removal to the sick bay slight spasms reappeared, upon which he was quickly transferred ashore." At the time of this man's attack, 7 p. m., the temperature in the open air was 82° F.

Dr. Grunwell calls attention to the sudden high temperature in some cases of malarial fever, and the absence of attacks in the hot dynamo room.

With this brief review, gentlemen, the question remains, What is Heat Exhaustion?

ETIOLOGY OF ELEPHANTIASIS.*

BY GEORGE CHEEVER SHATTUCK, M.D., BOSTON,

Assistant Physician to Out-patients, Massachusetts General Hospital; Physician to the Harvard Clinic.

Having recently become interested in sporadic elephantiasis through seeing a few cases, I undertook by a review of the literature to ascertain the present state of knowledge of this disease. Although much has been written about it, important questions of etiology remain obscure. Firstly, there are several types of elephantiasis, and several allied or similar conditions which merge with it in such a way as to render sharp distinctions impossible. Moreover, cases pathologically typical show striking differences in clinical history and in apparent etiology.

The term elephantiasis, as you know, formerly had a wide application. There was E. graecorum, now called leprosy, and E. arabum which included all other forms. Virchow regarded Madura-foot as a form of elephantiasis and was in doubt whether or not to include also fibroma molluscum. After this the application of the term became progressively narrower until a relation had been established between elephantiasis and filariasis. A tendency was then shown to regard the tropical cases as true elephantiasis and to speak of sporadic forms as pseudo (Brault) or false elephantiasis. This tendency met so much opposition from Hutchinson and others that sporadic and endemic cases are now included alike within the current meaning of the word.

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* Read before the American Society of Tropical Medicine, June 11, 1910, St. Louis, Mo.

There are several important varieties. One of the congenital forms involves the whole body. It occurs generally in acephalic monsters, and is due probably to congenital defect of the lymphatic system (Virchow). Elephantiasis lymphangiectodes and E. telangiectodes (Esmarch and Kuhlenkampff) resemble angiomata, are probably congenital and seem more closely related to tumors than to acquired elephantiasis. There is a similar cystic form (Virchow), a fibromatous form related to fibroma molluscum (Esmarch and Kuhlenkampff), and a neuromatous variety, but type cases of these have little in common with ordinary elephantiasis.

As this paper deals only with lymphatic elephantiasis, these forms need no further mention here.

Elephantiasis is again divided into groups corresponding roughly to etiology, — the congenital, the sporadic, and the endemic, — but until important questions of etiology have been settled, no classification on this basis can be satisfactory. The congenital cases present great variety. A few of them resemble so closely the common acquired forms as to suggest a similar etiology; but other cases are quite different, and so little is really known that I prefer to leave congenital elephantiasis out of this discussion.

Acquired cases of lymphatic elephantiasis are divided for descriptive purposes into elephantiasis of the legs, of the genitals, of the face and of the scalp. The older writers gave separate names to cases differing in external appearance or consistency. They distinguished thus, E. glabra, E. verrucosa, E. ulcerosa, E. mollis and E. dura. These distinctions do not correspond to essential differences.

Elephantiasis in the broader sense is not a distinct disease but a group of pathological conditions which leads to progressive enlargement of the part affected. How far this is true of acquired lymphatic elephantiasis is an important question. Undoubtedly, acquired elephantiasis is much the same in its clinical manifestations and in its pathology whether it appears endemically or sporadically.

The character common to typical cases of lymphatic elephantiasis is progressive enlargement. This enlargement is due to chronic edema, hyperplasia of connective tissue and dilatation of lymphatic vessels. The *central question* in the etiology of elephantiasis is as to the *relation between edema, hyperplasia* of connective tissue and *lymphatic dilatation*. To answer this question it is necessary to study independently the causes which may lead to each of these conditions.

Edema may be traceable to local or to distant causes of venous stasis; for example, to phlebitis; to chronic cardiac or renal disease; to disturbances of innervation, peripheral (Obersteiner and Redlich) or central (Edinger), as in polyneuritis or syringomyelia; to abnormal blood, as in anemia; to cachexia; or to inflammation. Experiments of Ranvier show that ligation of the femoral vein in a dog is not followed by edema unless the sympathetic fibers to the leg have been cut. Cutting the sympathetic causes arterial dilatation and increase of local intravascular pressure. Cornil and Ranvier believed this to be the real cause of edema, excepting perhaps the edema of cachexia. They say that if tension is sufficient, edema will occur even without obstruction of veins. They attribute the edema of inflammation to the same cause. Guyot[1] suggested trophoneurosis and Cornil,[1] interstitial neuritis as possible causes for the edema of elephantiasis. P. zur Nieden[2] believed that edema in elephantiasis was due to mechanical obstruction of lymphatic circulation, resulting from inflammation, and Lallement[3] attributed it to atony of vessel walls.

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[1] Quoted by Guillet.

Abundant clinical evidence shows that obstruction of lymphatics does not often produce manifest stasis of lymph, and Cohnheim's[4] experiments indicate that lymph stasis cannot produce *edema* if lymph formation is normal and if the veins are patent.

Therefore, the edema of elephantiasis is rarely if ever due to obstruction of lymphatics solely, but lymphatic changes may act as contributive causes of edema. It is important to recognize that venous thrombosis is commonly present in lymphatic elephantiasis, that proliferation of endothelium in the capillaries is one of the earliest changes (Winiwarter), and that this change favors obstruction. Edema in elephantiasis is influenced also by gravity. It begins generally in the legs and extends upward. In the earlier stages the edema is diminished by rest in bed and increased by walking.

Observation shows that chronic edema from almost any cause may form the basis for subsequent elephantiasis and that persistent edema is its first visible manifestation. In the majority of chronic edema, however, no elephantiasis follows. Kaposi says that edema with lymph-stasis is more likely to result in elephantiasis than is pure serous edema. From histological studies, Wernher concludes that the edema of elephantiasis begins in the skin.

We come now to the causes of varicosity and thickening of lymphatics, dilatation of lymph spaces and stasis of lymph. Virchow says that, in elephantiasis, obstruction and dilatation of lymph channels occurs early and that sometimes only the small, sometimes only the large, ones are affected. It has been observed earliest in the papillary layer of the skin (Winiwarter) and where the network of lymph capillaries is most extensive (Busey). When lymph channels are dilated, we may assume that there is some degree of lymphatic stasis, whether edema be present or absent, but experiments show that obstruction of large trunks, even ligation of the thoracic duct, does not always cause ectasis (Magendie, Dupuytren, Lesser[5]). Why changes in the walls of lymphatic vessels do not always follow retardation of lymph-circulation is explained by the rich anastomosis and the low pressure in the vessels. This is true especially of the smaller lymphatics (Fischer). Unna believes that lymph stasis can be produced only by hindrance to the escape of blood from the veins and that lymph stasis can under no circumstances produce extensive lymphangiectasis. He quotes various experiments to prove this. Moreover, ectasis occurs so frequently without obstruction of lymphatics that other explanations for it are needed. The following theories have been offered: that ectasis may result sometimes from proliferation (Langhans, Torock, Nasse[5]), that atony may cause it (Corre[6]), that congenital weakness or anomalies may predispose to it (Busey, Fischer), that gravity may be the chief factor (Wernher[7]), and that chronic heart disease with resulting venous and lymphatic stasis may produce it (Weigert[8]).

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[2] Quoted by Hastings.
[3] Quoted by Hastings.
[4] Quoted by Jarisch.

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[5] Quoted by Fischer.
[6] Quoted by Guillet.
[7] Quoted by Hastings.
[8] Quoted by Winiwarter.

Busey shows in his monograph that the etiology of lymphangiectasis and of obstruction of lymphatics is multiple, and that to account for it in some cases, a congenital change or an inherited weakness must be assumed. Fischer says that, owing to the disagreement of pathologists, no satisfactory conclusions concerning it can be reached. He himself believes that proliferation of lymphatic vessels is an important factor, but he agrees with the majority that lymphatic varices may result when, in a limited area, most of the lymph vessels are obstructed, and he explains that, by overfilling, the elasticity of the vessels is impaired, and that insufficiency of valves may result either from dilatation or from destructive inflammation. He compares the production of lymphatic varices to that of venous varices. It is generally agreed that the filaria can produce varices in the lymphatics, but the way in which it does this is purely conjectural. Winiwarter believes that ectasis of small lymph-spaces is the *first* change in elephantiasis.

Briefly, we have reason to believe that stasis of lymph may sometimes be promoted if not actually caused by obstruction or destruction of lymphatic trunks or glands, by agents acting from within or from without, by proliferation of the smaller lymphatics, by changes in the walls of the lymphatic vessels due to inflammation, or by widespread destruction or thrombosis of small lymphatic vessels. These conditions may be either acquired or in part at least congenital.

Clinical observation teaches that lymph stasis, or a probable cause for such, is often a demonstrable antecedent to elephantiasis. If not a forerunner, it appears in the early stages of the disease. Busey is justified in the conclusion that *lymph stasis is a necessary factor in elephantiasis,* but that the *mode of its production is not essential.*

The third process which always accompanies elephantiasis is hyperplasia. Winiwarter says that it takes place in the endothelium of capillaries in tissue that appears normal near the margin of elephantiasis. A definite increase of vessels has been observed (Welt, Langhans, Rindfleisch [8]). In the early stage round-cell infiltration is found along the veins, but not around the lymph-vessels. Dilatation of superficial lymph-capillaries and spaces is accompanied by proliferation of endothelium which leads gradually to obliteration of the deeper vessels. Capillaries, arteries and lymph vessels of the skin contain clumps of endothelial cells and coagulated fibrin, the nerve sheaths show increase of fibrous tissue, and inflammatory hyperplasia occurs in the glands (Cornil). Connective tissue hyperplasia is first apparent in the deeper layers of the skin. It penetrates thence into the subcutaneous tissue, especially along nerves and vessels, leads to atrophy of fat and muscle, and in extreme cases replaces them entirely. When the periosteum is attacked, the bones hypertrophy. In the earlier stages of elephantiasis all components of the skin except the elastic tissue may hypertrophy, but with further increase of connective tissue the other structures atrophy (Jarisch). Enormous increase of smooth muscle has been observed in the scrotum (Rindfleisch [9]), but the changes here are the same in general as those of elephantiasis of the legs. Virchow likens the cut surface in E. dura to bacon, says that it resembles a mass of scar tissue and that the essential change is progressive increase of connective tissue.

How can this proliferation be explained? Andral

[9] Quoted by Luitheln.

looked upon it as a "scirrhous degeneration." Virchow believed that an "irritative" condition exists from the first and that, in cases following venous obstruction, slight injury leads to inflammation. Wernher explained that chronic irritation results from decomposition of stagnant lymph, that this irritation leads to increased growth from the abundant building material, that "subinflammation," and finally inflammation, follows. Kaposi thought that stagnating lymphatic edema renewed by attacks of inflammation was the basis of connective tissue hypertrophy, and to lymphatic and inflammatory edema he attributed a high nutritive value. He could not explain why serous edema without inflammation is sometimes followed by elephantiasis. Inflammatory edema is characterized by a network of fibrin not seen in simple edema (Cornil and Ranvier). Busey and Jarisch accept the theory of increased nutrition through stasis, especially lymph stasis, and Kock [10] attributes hyperplasia to stasis combined with inflammation as in chronic suppuration, ulceration or eczema. It was pointed out by Winiwarter that elephantiasis is most apt to occur when repeated and long-standing arterial hyperemia has coexisted with impeded outflow of venous blood and of lymph. He attributed this hypertrophy to overnourishment, and considered stasis to be the most important predisposing factor. The stasis might be produced by any sort of mechanical obstruction or by chronic inflammatory hyperemia.[11]

These views were generally accepted until Bard [12] asserted that chronic edema *per se* could not cause a permanent increase of connective tissue. He attributed the sclerosis to inflammation, and advanced the theory that chronic thickening of cardiac valves, and sclerosis of the liver and kidneys, so often occurring with it, were all inflammatory and due to the same underlying cause; and that elephantiasis was a similar process.

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[10] Quoted by Jarisch.
[11] Winiwarter.
[12] Quoted by Guillet.

After the advent of bacteriology Achalme [12] attempted to explain the supposed chronic inflammation by maintaining that the streptococcus could remain latent in the tissues and be responsible also for the attacks of acute inflammation. Guillet and others [13] tested this theory by attempting to cultivate bacteria from lymph withdrawn in the absence of demonstrable inflammation, and by searching for bacteria in sections of tissue from elephantiasis. Their results were uniformly negative. In the presence of acute inflammation the streptococcus has been isolated from a great many cases of elephantiasis, and Prout has asserted that elephantiasis, whether sporadic or endemic, is due to streptococcus infection. The majority of recent writers recognize that the streptococcus plays an important part in the etiology of many cases of *sporadic* elephantiasis; but they follow Manson in believing that the filaria is the principal factor in *tropical* elephantiasis. Dufougeré, who spent five years in the Antilles, believed at first that all elephantiasis was due to streptococcus lymphangitis. While there he saw many patients who had had repeated attacks of lymphangitis, but the majority of them did not develop elephantiasis. Nevertheless, every one of his 62 cases of elephantiasis affirmed that the trouble began with lymphangitis. Dufougeré isolated a peculiar diplococcus from 9 cases, and attributed elephantiasis to that rather than to the streptococcus. At about the same time Le Dantec[14] isolated a similar diplococcus, but he considered the presence of filaria necessary for the production of elephantiasis and explained the later disappearance of the filaria as due to inflammation produced by the diplococcus. Various other organisms have been cultivated in a few instances (Renon, Sabourand, Brault).

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[13] Bernhard and Blumenthal.

Less than a year ago Dubruel published some very important work on elephantiasis. His observations extended over five years, and for three years he was in Tahiti or neighboring islands. In this region elephantiasis is common, but other manifestations of filariasis, such as chyluria and varicose groin glands, are rare. Specimens of blood taken in the evening from 200 cases, about one eighth of the total population in the island of Moorea, were negative, although elephantiasis occurs there in about one twelfth of the population. No case of chyluria was seen, and no filaria was found by examination of centrifugalized lymph from cases of elephatiasis which had been operated on. The filaria was observed only in a single case which had been sent to the hospital with the diagnosis of typhoid fever.

Blood withdrawn in the absence of fever from outside the diseased area in cases of elephantiasis gave no growth on ordinary media, but at the height of an attack of lymphangitis, blood from any part of the body yielded staphylococci in pure culture. Fluid taken from old cases that had not had acute inflammation for years generally gave no growth. Fluid withdrawn in the presence of lymphangitis showed streptococci more frequently than that withdrawn between attacks. Sometimes the fluid showed also staphylococci, but they were not infrequently mixed with other organisms. Two kinds of bacilli and a diplococcus are mentioned.

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[14] Quoted by Dufougeré.

Important evidence points to the possibility of contagion in elephantiasis.

Dubruel's conclusions are as follows: That it does not appear that the filaria plays the part in elephantiasis attributed to it by Manson; that tropical elephantiasis should be brought closer to elephantiasis nostras, a bacterial disease following repeated erysipelas, and that during acute attacks of lymphangitis patients should be regarded as infectious and should not be admitted into open surgical wards.

From regions where the filaria and its intermediate host abound, Manson presents evidence proving that the filaria is an important factor in the production of elephantiasis. That it can cause dilatation and varicosity of lymphatics is probable. That it can of itself produce inflammation or fever is not proven. Manson says that, by injuring the lymphatics, the filaria predisposes to bacterial infection and that to infection the lymphangitis and fever are due.

It is undeniable, at any rate, that inflammation of bacterial origin often precedes, and generally accompanies, the development of elephantiasis wherever found. Doubtless in many cases inflammation plays an essential part in causing hyperplasia of connective tissue. The view that hyperplasia in elephantiasis may sometimes result from chronic non-bacterial irritation, or from hypernutrition in the absence of inflammation, is questionable, but many cases in which bacterial inflammation was never manifest can be cited in its favor. To explain this group of cases, and those in which elephantiasis develops after a single inflammatory attack, congenital anomalies or weakness of lymphatics may be inferred. On the other hand, it has been suggested that the congenital cases which resemble acquired elephantiasis may be due ultimately to intra-uterine infection.

SUMMARY.

1. The essential characteristics of typical acquired elephantiasis are lymphangiectasis, hyperplasia of connective tissue, and chronic edema.
2. The relation of these to each other in the production of elephantiasis is not clear.
3. It appears that these changes may frequently be attributed to the interaction of stasis and of inflammation.
4. Stasis always occurs early and persists.
5. Inflammation may precede or follow stasis, or may not be manifest at any stage of the disease.
6. Inflammation when present may be acute or chronic; and is generally traceable to bacterial infection.
7. Either chronic stasis or inflammation from any cause may predispose to elephantiasis, but even when they occur together, elephantiasis does not always result.
8. There is reason to suppose that congenital weakness or anomalies of lymphatics may play an essential part in the production of some cases of elephantiasis; and that such weakness or anomalies can be inherited.
9. The filaria is an important factor in the production of endemic elephantiasis of some regions, but it is not essential to the occurrence of endemic elephantiasis.
10. Elephantiasis in filarial regions results indirectly from filariasis through bacterial infection.
11. Sporadic lymphatic elephantiasis and endemic elephantiasis are not essentially different.

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UNSOLVED HEALTH PROBLEMS PECULIAR TO THE PHILIPPINES.*

By Victor G. Heiser, M. D.,
Manila, P. I.,

Director of Health for the Philippine Islands; P. A. Surgeon, P. H. and M. H. S.

(*Under the Imprimatur of the American Society of Tropical Medicine.*)

Many of the modern problems of hygiene and sanitation are the same the world over whether found in tropical or temperate zones.

There are certain characteristic phases of tropical hygiene and sanitation, however, which have received most gratifying attention in recent medical literature and which we cannot but interpret as a very general interest and desire to make these portions of the world compare well in healthfulness with those heretofore believed to be more favorably situated. But in addition to these general problems, common to all tropical countries, there are additional difficulties and handicaps peculiar to each country or peoples, which have required special consideration.

It is the object of this paper not only to present the problems and theories with which you are already familiar, for it is desirable that you should know what we also are doing along these lines, but more especially to put before you the peculiar conditions which have seemed to hinder our more rapid progress and which are still blocking the way to

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better sanitation and hygiene in the Philippine Islands.

In general, we have first a poverty stricken people with a poor physical inheritance, people strongly imbued with superstitions and habits, the antithesis of the simplest health doctrines and practices, a people lacking ambition to till in an active manner the fertile soil, a people the masses of whom are apparently content in their ignorance and poverty and resigned to and uncomplaining of their many ailments. Work among them is handicapped by the inaccessibility of many of the islands, roads which though being improved at a remarkable rate, are yet unfit for travel in many instances during portions of the year. It is further handicapped by the lack of a common language, for many dialects are spoken among the tao or peasant classes to whom neither Spanish or English is intelligible. It is handicapped by the lack of medical employees who are sufficiently interested in the cause of humanity to undergo the innumerable hardships and discomforts which accompany most of the health work in the provinces. Untold credit is due those who are at present carrying on the work the burdens of which fall more heavily upon them because of their limited numbers. We are also handicapped by a treasury of which it is quite possible at times to see the bottom, so that it is not put to us "do all you can regardless of expenditure," but "your expenditures must not go beyond this or this; do the best you can with it." So our very largest problem is that of discrimination; shall we devote our energies to this question or that question? we cannot do all; shall we attempt this one and abandon that, or do a little toward each? Thus far it has been our policy to do a little toward each.

Malaria.—The malaria problem is a very large one. For instance, in the province of Ambos Camarines, which has a population of 233,472 persons, there were 745 deaths from this disease reported for the year ended June 30, 1909. A conservative estimate of ten cases for each death with an illness of ten days makes 74,500 days loss, which, valued at only $0.25, United States currency, a day, would amount to $37,250 a year; this being for only one out of thirty provinces, we can conservatively multiply it by twenty, which would make an economic loss to the country of $745,000. If a human life can be economically valued at $1,000 or $500 or $100 in this country, making deductions for children, etc., we find ourselves confronting a loss of at least $5,000,000 per annum from this disease alone, and yet this represents a small portion of the total loss which can be attributed to preventable diseases.

The number of malarial cases has been greatly decreased, however, by instituting drainage wherever possible, by the free distribution of quinine, and by campaigns of education, particularly in the schools where pupils are taught the value of mosquito nets, the danger from mosquitoes, and how they may be destroyed, etc.

Mosquitoes.—There has recently been an active newspaper agitation concerning the eradication of mosquitoes in Manila, but few persons realize the obstacles that block our way in such an undertaking. Manila is on low land, much of its area being below sea level in fact. To bring the city to a drainable level would be a necessity in such a proposition, and is estimated to cost $4,000,000 at least. When we reflect that the annual income of the city is under $3,000,000, we naturally pause before recommending a measure which would be so costly, especially when some authorities consider such an undertaking problematical, and more especially since there is practically no reliable data on hand to show that the mosquitoes of Manila are responsible for the transmission of disease. We can well imagine how a similar proposition would be received in the United States or any other country. Should we expect it of these islands, overburdened as they are with more acute problems? It seems to the writer more logical to begin mosquito elimination in Manila, at least, by educating the individual householders to make the breeding of mosquitoes on his premises impossible, and then by an organized inspection service enforce regulations which will compel the use of such knowledge. In the meantime a definite engineering project should be adopted and drainage, filling, and oiling should be carried out with the regular sanitary force as far as possible.

Water supply.—The water supply of the Philippines is another serious question. All surface waters found in the islands except the thermal or those strongly charged with certain minerals are amœba infected. Improved health conditions in Manila can to a certain extent be traced to the new city water supply, which now comes from a comparatively uninhabited watershed, but even as tap water it should be boiled for all but the most ordinary purposes. Fortunately, artesian well water is as a rule free from amœbæ, and is in every way an ideal drinking water. In towns where artesian well water is almost exclusively used the death rate has fallen fifty per cent. These wells are being drilled as rapidly as possible, but there are many localities where they are impracticable, so that the question of how to make available for the people an unlimited and safe water supply exclusive of artesian well water must be considered one of our unsolved problems.

Disposal of excreta.—We are still pondering the practical disposal of excreta. Many plans have been proposed, all more theoretical than practical. Of those who are familiar with local conditions and who realize the resources and limitations of the average community, but who are seriously searching for a practical solution, none as yet have put forth a well defined scheme.

In large communities where water carriage of sewage is possible, septic tanks are used successfully. In communities in which cholera has prevailed, the pail system, the digging of pits, and covering of excreta with lime or clean earth at regular intervals, has been found effective, but the cost of maintenance of inspection is prohibitive and only warranted by emergency conditions.

Some years ago the writer suggested a plan of installing a pail system with an after treatment of the night soil which would render it suitable for fertilizing mulberry trees, thus promoting the silk industry, the income from which would in a short time place this particular sanitary measure upon a self paying basis.

The plan followed in many Oriental countries of letting out private contracts for the collection of night soil from private residences is not believed to be a safe one. It is an established custom to use such night soil for fertilizing vegetables, and it is believed that the consumption of such raw vegetables thus fertilized has had much to do with the spread of amœbic dysentery, cholera, hookworm, and other intestinal diseases.

Smallpox.—Smallpox, once so formidable a proposition to us, has at least been reduced to insignificant proportions. Over 6,000,000 persons have been vaccinated by the Bureau of Health within the past five years. The unvaccinated are in remote regions where as yet it has been found impossible to convey vaccine in a potent condition.

The ordinary glycerinized lymph at present in use will not keep for more than from seven to ten days at the temperature which prevails here. As many of the sections to be reached are in traveling time from two to three weeks away from the point to which ice can be sent or cold storage is available, it is obvious that a vaccine is necessary which will retain its potency for a longer period of time than any now obtainable. Vaccine in powdered form has been tried, also dry points, but the percentage of success is so small and danger of infection so great that their use is restricted.

The acute phase of this problem then is either to manufacture a more effective vaccine or to find a way of transporting it successfully. Observations point to the conclusion that ordinary cowpox vaccine is not as effective in the dark as in the white skinned races. The writer has personally observed that out of more than one hundred cases of smallpox or varioloid among white people, not one case occurred in a person who had been vaccinated within five preceding years, while there have been many cases of smallpox among Filipinos of whose successful vaccinations within one preceding year there could be little doubt.

It has been interesting to observe a demonstration of this at Bilibid Prison, where all prisoners are vaccinated upon admittance, and regularly once a year or oftener thereafter. Yet smallpox has made its appearance there each year and many cases have occurred in persons who show the typical pits accepted as characteristic of previous attacks of smallpox.

Tuberculosis.—Tuberculosis is another of our problems. We estimate that it claims as many victims here as in other portions of the globe, and it will require the same activity here as elsewhere to hold it in check. The introduction of outpatient tuberculosis dispensaries, the construction of shacks in the mountains, the opening of night camps near Manila, arrangements for the hospitalization of the helpless sick, and prophylactic instruction in the public school, the usual methods in fact that are employed elsewhere, are now under way here; but the tuberculosis problem has its peculiar and complicating features in the Philippines, viz., the unsuitable dietary of the people, their peculiar superstitions concerning the contraction of the disease, their almost unshakable fear of night air as a poisonous thing, a fear which has kept their houses tightly closed at night for generations past, their habit of chewing betel nut which has made the custom of expectorating in public and private a universal and, we sometimes fear, an unbreakable habit. Added to this is their utter resignation to the disease as a thing incurable and inevitable. Therefore not only have we the ordinary preventive and curative measures of tuberculosis to organize and enforce, but we must devise ways of cooking and preparing native products into a suitably nourishing and popular dietary, and then educate the masses into not only the ways of doing it but to an earnest desire for it. They will have to be first cured of their superstitions, which is as great a task as converting them to a new religion; houses will have to be opened at night, betel nut gradually abolished, and then a gigantic antispitting crusade begun, and last of all comes the Herculean task of rousing them out of their inertia and convincing them that not only is tuberculosis curable, but that they are responsible for the spread of the disease and able to themselves accomplish the cure.

Cholera.—Cholera is still with us in spite of the active measures which are constantly being taken to eradicate it. Though we have been so far successful in promptly suppressing outbreaks, whenever they appear, yet it is constantly occurring in sporadic form over widely separated sections of the islands. The puzzling question is this: When no possible connection with any previous case is discoverable, where are the cases of cholera contracted that appear so spasmodically over these widely separated regions? Where it is lying dormant during the periods of time when no cases are reported is yet to be determined. Some years ago the writer drew attention to the fact that logical deduction indicated that there was a morphological change in the cholera organism which made it difficult to recognize at certain stages. Research work done in the meantime strengthens this view. There is also a strong probability that cholera carriers are responsible for some outbreaks. Yet the fact remains that the disease appears frequently at places the origin of which cannot be satisfactorily proved.

Plague.—Plague at present is a stranger to the Philippines. Measures for its eradication were begun in 1900, but it was not until the scheme of dealing with rats heretofore described was used that the disease disappeared. Since April, 1906, no cases have been found in human beings, and no cases in rats since 1907.

On account of the close proximity of China, however, where plague seems to appear every year, special precautions are constantly taken at our ports in order to prevent the reintroduction of this disease. The question, of course, is how to safely accomplish this with a minimum amount of annoyance and loss to the shipping interests and to the travelling public. The present plan is to fumigate all vessels from infected ports twice annually and to keep the interisland vessels free from rats and vermin by systematic fumigation in order that the plague may be at once checked, if by any accident introduced. Wharves have been made rat proof and vessels where docked are required to use rat funnels in order to keep rodents from gaining access to the shore. At the port of departure for these islands vessels are inspected by medical officers of the United States in order to ascertain that there is no plague aboard.

Typhoid fever.—While cases of typhoid fever are undoubtedly contracted in the Philippines, yet it can hardly be said to be prevalent here. To prevent its establishing a foothold regulations were prepared for disinfection of excreta from such cases, for the protection of water supplies, and regulations concerning inspection and sale of milk, also by sanitary measures for the eradication of flies. Whether further and more stringent precautions could be taken at this time or are practicable is a question for consideration.

Infant mortality.—The subject of infant mortality is a vast one. In Manila approximately one half the total number of deaths occur in children under one year of age. From papers read at this meeting and previously it is obvious that the largest share of it is due to improper nourishment. The poverty of the people makes properly marketed cow's milk either fresh or canned an impossibility unless given to them in the form of charity. This for the great mass of people is not only impossible but undesirable. How to bring a cheap milk supply within the reach of the poorer classes seems to be the acute phase of the infant mortality problem. The raising of goats would seem to be the solution. Already experiments in breeding a hardy variety of milk goats have been inaugurated. This problem must not be abandoned, but be rapidly pushed to a solution, for, left unsolved, it involves the heaviest mortality we are at present facing.

Putrefactive changes in foods.—Another complicating feature and cause of illness in the tropics, particularly in the Philippines, is the putrefactive changes in nitrogenous foods, which take place so rapidly in warm climates. The problem is either to provide ways properly to preserve such foods or to find suitable substitutes which will enable us to eliminate them from our tropical dietary.

Unsanitary habits.—The food question brings in its trail another problem that is peculiarly ours and which we know to be the largest factor in the transmission of cholera and intestinal diseases. This is the native and almost universal habit of eating with the fingers. Proper example has done much and the distribution of literature on the subject has helped; but the masses are as yet untouched by either example or precept, and we see years of discouraging struggle ahead of us before they can be broken of so fixed a habit, the menace of which is as yet entirely beyond their comprehension.

Poor statistical information—So much for the particular problems. The entire situation is hindered by our inability to secure proper statistical information. This is due to a lack of officials in the provinces sufficiently skilled to make reliable reports on the causes of death. Whether the municipal officials can be trained and educated to do this remains to be seen. As I told you in the beginning, our work is first one of discrimination, a placing of our heaviest artillery where the enemy is strongest. This we cannot always determine on account of the inaccuracy and incompleteness of available data.

SUMMARY.

To summarize, it is to be understood that the health of these people is the vital question of the islands. To transform them from the weak and feeble race we have found them into the strong, healthy, and enduring people that they may yet become is to lay the foundations for the successful future of the country. But it is not alone the problem of the Bureau of Health. It is an economic and educational question as well. Every branch of the government has its part to perform, and cooperation is essential. Good roads, agricultural improvements, the elimination of rinderpest and other animal diseases, the general development of the country which will gradually bring about a better standard of living, education, particularly along the lines of hygiene and sanitation, to which we give all the aid possible, but for the dissemination of which we will have to depend upon the teachers and the public schools, the special training of the young men and women of the islands in the professions of medicine and nursing, all the foregoing factors with which we, as a bureau, have nothing to do, are as important to the health conditions of the islands as is the actual holding in check of epidemics and disease, the sanitary inspections, enforcement of regulations, etc., the opening and maintenance of hospitals throughout the islands, and the various other things for which the Bureau of Health is directly responsible.

The government is not a rich one. How to do the most and the best with a limited income is still an acute question. You can see what an enormous proportion of that limited income it would take to carry out successfully any one of the various health projects enumerated. To give thorough attention to a particular one would involve an unwarranted neglect of the rest. We have hence concluded we must do the best we can with the entire proposition, going slowly but making headway each year, each month, perhaps each day.

It should be remembered that much of our appropriation is consumed in ways unusual for a health bureau. The maintenance and management of government hospitals falls to our lot and is no small burden. We are practically cleaning up these islands, left foul and unsanitary and diseased by generations of hygienically ignorant peoples. We are stamping out the conflagration of disease started long before American occupation, and not until it is stamped out can we look forward to the modern problems which come so temptingly before us. And so, much of our time, money, and effort is being constantly consumed in works, the glory of which is still behind the clouds. We are draining the land, as it were, before beginning the constructive health projects, which are going to make these people the strong and healthy race we intend them to be.

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UPON THE PRESENCE OF SUPPURATION IN THE TUBERCLES OF LEPROSY.*†

FRASER B. GURD.

(From the Pathological Laboratory, Tulane University of Louisiana.)

Altho the majority of leprographers recognize that the cutaneous nodules in the tubercular type of leprosy may and do occasionally "break down" with the formation of a purulent or necrotic material, resulting in many cases in sinuses or ulcers, practically all observers are unanimous in stating that true pus formation or polymorphonuclear leukocytic invasion of the tubercles occurs only in the presence of a secondary bacterial invader such as the streptococcus or staphylococcus.

Sticker[1] remarks that there can be no suppuration without the presence of pyogenic cocci. Babes[2] considers the "breaking down" to be a true necrosis, and trophoneucrotic in origin. In a similar manner by all authors except Sugai,[3] the possibility of acute inflammatory processes on the leprous lesion is either neglected or denied.

This last-mentioned author reported in 1909 a series of cases, in which pus was found in the nodules, in one of which no organisms other than the leprosy bacillus were found. His methods of excluding the possibility of secondary invasion were somewhat incomplete in that cultivation was not attempted. He states, however, in his conclusions that the leprosy bacilli may cause suppuration without the presence of any pyogenic coccus.

That many or, perhaps, most of the abscess formations, suppurative arthritises, and other purulent processes occurring in leprous patients are due to the invasion of tissues whose resistance is lowered by one or other of the ordinary pyogenic bacteria is undoubtedly correct; that, however, such a condition is not a necessity the following case which came under the author's observation proves.

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† Read by title at the seventh annual meeting of the American Society of Tropical Medicine, held at the Medical School of the St. Louis University, June 11, 1910.

[1] *Tropen-Krankheit* (Mense), Leipzig, 1905.

[2] *Nothnagel Encyclopaedie,* Wien ("Lepra").

[3] *Lepra* (Leipzig), 1909, 8, No. 3.

The patient, a young white male of 22 years, had suffered from leprosy during a period of between two and three years. During this time he had passed through several attacks of exacerbation of symptoms consisting of high fever, with swelling edema and reddening of the tubercles. Upon the occasion when seen by the author his temperature had been between 103° and 104° F. for three days. He was suffering from malaise anorexia and other evidences of a constitutional disturbance. The tubercles situated over the face and hands were much swollen, very red and tender: one swelling over the malar prominence on the left side had ruptured spontaneously and was discharging pus. A tubercle over the posterior surface of the left wrist was incised, resulting in the expulsion of about 25 c.c. of a yellowish-green purulent material.

This material was planted upon the ordinary and several special culture media, both aerobically and anaerobically, without the development of a single colony.

Smears were made and stained by Giemsa's method, carbol fuchsin with acid decolorization, and by Gram's. The cellular elements with the polychrome stain consisted almost exclusively of polymorphonuclear leukocytes, together with a small number of large vesicular nuclei, practically devoid of protoplasm. Leprosy bacilli were present in very large numbers. A few well-formed aggregations or globi were found, but for the most part the bacilli were lying singly or in small groups. A much larger percentage than usual appeared broken up in the form of granules. Certain numbers of pus cells contained a few bacilli, but in general the organisms were free. Absolutely no other bacteria could be demonstrated in any preparation.

In addition to the above case in which comparatively large pus collections were present, the routine examination of a number of leprosy nodules derived during life and at autopsy has shown that polymorphonuclear leukocytes may be found almost constantly in small numbers, although in no case have definite foci of such cells been seen.

The fact that acute exudative inflammatory changes should occur in leprosy is not strange when we consider the other granulomata, such as tuberculosis and glanders. Acute abscess formation in tuberculosis is not frequent, but can hardly be said to be rare, and a moderate number of pus cells may be found in many lesions. As demonstrated by Duval,[1] working upon glanders in laboratory animals, all lesions from the acute to proliferative may be produced by varying the virulence of the organisms used.

An interesting observation, with reference to the clinical course of cases which develop the so-called lepra-fever, has been made by Dr. Ralph Hopkins of this city; namely, that immediately following the cessation of the attack the condition of the individual improves until both constitutionally and locally the patient is better than previous to the onset of acute symptoms. This condition of affairs occurred in the case described in this paper.

It is difficult to understand why the invasion of the lesions by acute inflammatory cells should take place in this sudden manner, but there would appear to be no doubt but that the action of these cells results in a destruction of many of the bacilli with consequent clinical improvement. The author considers that a routine examination of tubercles from cases of lepra-fever would in all probability show a comparatively large proportion of polymorphonuclears.

Since it does not seem reasonable that an alteration in virulence should suddenly take place simultaneously in the bacilli in lesions in different parts of the body, the cause of the alteration in the reaction to the irritant must be looked for in the individual suffering from the disease. In studying the local cellular changes in such cases, therefore, the opsonic index ought to be considered, for, since we know that the opsonin influences the phagocytic activity of the polymorphonuclear leukocytes, we should expect to find the index against *B. leprae* raised at the time during which the cells are more active. That this increased reaction is potent to injure the organisms, the degenerative condition morphologically of the organisms and the improvement of the disease clinically are evidence.

[1] Duval, *Jour. of Exp. Med.*, 1907, 9, No. 4.

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SOME UNDERLYING CAUSES OF THE EXISTENCE OF SOIL POLLUTION IN RURAL DISTRICTS.*

By CH. WARDELL STILES, Ph.D.,
Professor of Zoology, U. S. Public Health and Marine-Hospital Service.

Recent investigations have shown that in our rural districts there is a great amount of soil pollution, and attention is turning to this insanitary condition in connection with the campaigns that are being carried on against certain diseases, especially typhoid fever and hookworm disease.

According to a recent summary of statistics of 4,825 farmhouses, tabulated for six states, 55 per cent have no privy of any kind; of 2,499 farmhouses, tabulated as occupied by whites, 35.3 per cent are without a toilet, and of 2,326 farmhouses occupied by negroes, 76.8 per cent have no privy.

The average reader may perhaps consider that the foregoing statistics of the extent of soil pollution in the rural districts are somewhat exaggerated. To this it may be replied that the conditions described are from actual observations, and attention may be invited to the further fact that no detailed account has been given of the actual condition of the privies which exist on those farms that are provided with them, nor has the point been emphasized that even when privies are present, frequently they are not used, especially by the male members of the family.

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*At the request of Dr. Charles P. Neil, Commissioner of Labor, an investigation into the prevalence of hookworm disease in the cotton mills was undertaken. Certain portions of the results obtained will be published in the reports to be submitted to Congress by the Bureau of Labor, while the more strictly medical discussions will be published elsewhere. The present article represents one in the series to be issued.

*Names and localities are purposely suppressed.

When such a widely spread custom (or lack of custom) exists, there must be some explanation for it, and in seeking to analyze the conditions the following points have come to my attention.

In the first place, while this pollution is greatest among the negroes, and among the tenant whites, it is by no means confined to them.

In a certain American college* there is an interesting chapter on the subject of soil pollution. It should be recalled that we are dealing here with college students, yet the President of the college told me it had been so difficult to induce certain of the boys from the country districts to use the regular water closets in the college buildings that he had been obliged to build a privy on the college campus in order to protect the campus from promiscuous fecal pollution. This privy was open in back and presented excellent opportunity for the spread of disease.

A certain United States official has recently been stationed at a certain college* for males. He informs me that one of the departments of this college has no toilet of any kind, and that the students practice soil pollution along the sides of the building.

A well known and very prominent educator* assures me from personal experience that there is a certain co-educational institution* for adults which had no toilet room in one of its buildings until a few years ago. Sometime ago I had personal knowledge of one other case of this kind (also a co-educational institution), and I personally witnessed soil pollution back of the dormitory.

One of the best known educators* of the entire country recently stated to me that about 30 per cent of the country schools of his state* had no privy. Personally I have seen a number of country schools and churches without privies.

A person who has made a special study of the schools in one state* assured me recently that in one section of that state it was the exception that country schoolhouses had a privy.

In two states*, in the hearings of ex-President Roosevelt's Country Life Commission, testimony was given to the effect that, as a rule, in certain districts, neither the country churches nor country schools had toilet facilities of any sort. In another state,* one of the state officials described the sanitary conditions on the farms as "simply atrocious;" in still another state,* a member of the State Board of Health described them as "awful."

Among many prominent and educated lawyers and even among physicians, I have found a prejudice in favor of promiscuous defecation.

There are, it seems, several factors which explain at least a part of this widespread disregard of sanitary precaution.

1. *Hot Climate*—With the hot summer days the ordinary surface privy becomes a place of foul odor and filled with flies, especially if not regularly and frequently cleaned. It is, therefore, a place which a person naturally wishes to avoid, hence he naturally seeks the open, with better air.

2. *Influence of the Negro, Mexican and Indian*—The negroes, Mexicans and Indians are much nearer primitive man than is the white, and it need not therefore seem strange that these races are greater soil polluters than is the white. The servant class in the South is composed almost exclusively of negroes, and the influence exerted on the white children by the negro nurse is apparent in more ways than one. It is expecting almost too much of the average negress that she will of her own accord instill into the white children ideas of personal habits which are rather foreign to her own training. Many white children are actually trained by their negro nurses into the habit of soil pollution, and the habit remains with them, to some extent, in later life.

3. *Influence of Hookworm Disease*—A person who has a severe infection of hookworm disease is not predisposed to making any unnecessary effort to find a privy when a more or less secluded spot may offer to him a safe retreat. While soil pollution favors hookworm disease, the converse is also true; hookworm disease favors soil pollution.

4. *Economy*—If one visits the hovels in which many of the rural tenants live, one is seriously impressed by their inferior condition. It is not very uncommon to find a family living in a one-room or two-room hovel, and in many instances the entire family, including brothers and sisters from 1 to 18 years of age, or older, eat and sleep in one and the same room. The same conditions of poverty that give rise to such economy would naturally result in economy in respect to building privies.

5. *Economy in Time and Work*—A poorly kept privy is not only an eyesore, but is an exceedingly unpleasant thing to have near a house. To avoid this unpleasantness, it is necessary to clean the privy regularly. This takes both time and work, and it is not a prominent characteristic among either the rural white tenants or the negroes, Mexicans and Indians, to devote any special amount of time to work which is not only disagreeable, but for which they see no necessity.

6. *Popular Beliefs*—There seems to be a more or less widespread idea among these country people that it is much better to scatter the night soil around than to collect it in one place. Two alleged advantages occur to their minds in support of this view, namely: (a) it is thought that the action of the sun is a powerful factor in destroying any injurious effects arising from night soil; and (b) it is thought that the night soil is valuable as fertilizer.

The first idea (a) is not without a certain amount of foundation; still, as a practical fact, people are prone to defecate in shaded places, hence the sun is not likely to exercise its disinfecting influence; further, the fact of the escape of thousands of hookworm embryos into the soil, whereby they avoid the action of the sun, is unknown to these people.

As for the second idea (b), without going into the question whether night soil is such a valuable fertilizer as is popularly supposed, the point may be raised that if the material is allowed to ferment sufficiently long or is boiled before being on the ground, the sanitary dangers involved are avoided.

7. *Popular Ignorance Regarding Sanitary Matters*—There is a widespread ignorance as to what constitute proper sanitary conditions, and this ignorance is especially marked among government employees, free delivery men (especially postoffice employees), and farmers. Thus in a recent inquiry the fact was developed that of 77,127 persons, 56,893 persons, or 73.7 per cent, were unqualifiedly satisfied with their sanitary conditions (despite a nation-wide typhoid death rate of 46.5 deaths per 100,000 inhabitants, according to the twelfth census)!

8. *Low Rental of Farms*—Many of the tenant farms are not giving the returns which the landlords think they should, and the owners are not therefore inclined to expend more money for improvements than seems necessary to them. As their knowledge of the dangers of soil pollution is not much greater than the knowledge possessed by the tenants, the necessity for the building of sanitary privies is not apparent to the owner.

9. *Privacy*—As the popular conception of a privy is that it is a place for privacy, and as the chances for privacy are greater in sparesly populated areas, as away from the main roads, than in more densely populated localities, the popularly accepted reason for the existence of a privy is not self-evident to the inhabitants in the outlying districts.

From the foregoing it may be seen that soil pollution can, at least to some extent, be explained, and the very fact that there are certain definite reasons which tend to keep the custom alive shows us the importance of conducting an intelligent campaign against this pernicious evil.

Soil pollution is in the nature of *"malum in se";* it is an "aggravated offense against the public welfare;" *ergo,* it should be made a "crime," and as such it should be punished by law.

THE PREVALENCE OF HOOKWORM INFECTION IN THE BETTER CLASS OF SOUTHERN WHITE PEOPLE

J. G. GAGE, M.D., AND C. C. BASS, M.D.
NEW ORLEANS

We offer the results of this investigation as an indication of the prevalence of hookworm and other worm infections among the better class of people in the South. Statistics are at hand showing the prevalence among army recruits, hospital patients, laborers and the poorer class, but statistics showing the prevalence of the disease among the upper classes are wanting. Recently Winthrop examined sixty-six students in the Mobile Medical College, of whom thirty-three, or 50 per cent., were found infected.

Dr. Dock suggested the examination of the students of Tulane University because the results might serve as an index of the prevalence among apparently healthy individuals representing a large area of the South.

The total number of students examined was three hundred and fifteen. Of this number one hundred and four, or 33 per cent., harbored intestinal parasites; seventy-nine, or 25 per cent., were infected with hookworms. There were also nineteen cases of infection with *Trichocephalus,* five *Strongyloides,* five *Hymenolepis nana,* and one *Tænia saginata.* We were unable to separate students residing in cities from those residing in the country and smaller towns, except in the case of New Orleans students. Of two hundred and fifty-nine students not residents of New Orleans seventy-eight, or 30.1 per cent., were infected with hookworm.

Table 1 gives the results by states. New Orleans students are classed separately. Students who had lived in the country or small towns when children and had since moved to New Orleans are not classed as New Orleans students.

From this table it is seen that a large proportion of the students from Louisiana, Mississippi, Alabama, Georgia, Texas and Arkansas were infected with hookworms. The other southern states have such a small representation that the negative findings carry little weight.

Many students, on hearing that others from their towns or states were infected, took a course of thymol on their own responsibility without first having their stools examined. Some of these gained weight afterward, several as much as ten or fifteen pounds. Some of them, no doubt, would have shown infection if the examination had been made before they took thymol.

Double infections were not frequent, only six being found; three with hookworm and trichocephalus, one with trichocephalus and hymenolepis, one with hookworm, hymenolepis and strongyloides and one with hookworm and *Tænia saginata*.

For most of the work slides 2 by 3 were used, the spreads covering as much of the slide as was convenient to handle and examined with a low power objective without cover-glasses. From one to four such preparations were carefully examined. In ninety-two of the specimens five ordinary 1 by 3 slide preparations were examined by each of five different men. By this method hookworm eggs were found in forty-one specimens. All specimens negative by this method were examined by the special method described[1] by one of us. Of two hundred and seventy-four specimens which were negative by the ordinary method of examination, thirty-eight, or 13.8 per cent., showed hookworm eggs by this method.

TABLE 1.—INTESTINAL INFECTION AMONG STUDENTS AT TULANE UNIVERSITY, BY STATES

States.	Total.	Negative.	Hookworm.	Trichocephalus.	Strongyloides Intest.	Hymenolepis Nana.	Tenia Sag.	Double Infection.
Louisiana	86	47	27	10	2	3	..	(1-2) (2-4) (1-3-4)
New Orleans	55	47	1	4	1	1	1	....
Mississippi	55	38	14	1	1	1	..	....
Alabama	34	19	14	1	..	..	..	....
Georgia	14	7	7	..	..	..	..	....
Texas	24	17	7	1	..	..	..	....
Arkansas	13	9	4	..	..	..	..	....
Tennessee	10	6	2	1	1	..	..	....
Oklahoma	4	3	1	..	..	..	..	....
Florida	5	4	1	..	..	..	..	....
South Carolina	2	2	..	..	..	..	..	....
Kentucky	1	1	..	..	..	..	..	....
Missouri	3	3	..	..	..	..	..	....
Illinois	2	2	..	..	..	..	..	....
Pennsylvania	1	1	..	..	..	..	..	....
Massachusetts	1	1	..	..	..	..	..	....
Canada	1	1	..	..	..	..	..	....
Mexico	2	2	..	..	..	..	..	....
Porto Rico	1	...	1	1	..	..	..	(1-2)
Roumania	1	1	..	..	..	..	..	....
Total	315	211	79	19	5	5	1	4

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[1] Bass, C. C.: Some of the Difficulties in the Diagnosis of Mild Hookworm Infection, Louisville Month. Jour. Med. and Surg., 1910, xvi. 277.

Of the ninety-two specimens in which twenty-five slides of each were examined, twenty-four were found to contain ova. When the negative specimens were properly centrifuged and examined eight others were found infected. Therefore 25 per cent. of the positive cases were missed by the examination of twenty-five slides by the ordinary method. Table 2 gives the results by both methods:

TABLE 2.—RESULTS OF PARALLEL STOOL EXAMINATIONS BY TWO METHODS.

Method.	Hookworm.	Trichocephalus.	Strongyloides intestinalis.	Hymenolepis nana.	Tænia saginata.
Ordinary method...........	41	3	4	3	..
Bass' method, cases missed before....................	38	16	1	2	1

It is evident that many mild infections are overlooked in the ordinary method of stool examination, since about one-half of our series were found by the special method. We have come to the conclusion, however, that for ordinary purposes the calcium chlorid solutions as described by Bass[2] are unnecessary. Washing with water alone is sufficient unless one wishes to get the eggs as free from débris as possible, when the calcium chlorid solutions are very useful.

Only four of forty-seven of the infected students whose history was obtained on this point gave a negative history as to ground-itch. Six others were not sure; the rest gave a positive history of ground-itch from six months to fifteen years before. The majority of non-infected students also gave a positive history; exact figures are wanting, but those giving a negative history were few.

No student examined considered himself ill, and very few of those infected with hookworm presented symptoms. However, it occurred so often that it became the rule that when the investigation was started on a new class or department, very few of the first to present themselves for examination were infected, but of those from whom it was difficult to get specimens for examination, either because they were sure they were not infected or were not interested enough to find out, a much larger proportion were infected.

Table 3 shows the comparative blood findings in sixty-six of the cases.

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2. Bass, C. C.: Mild Uncinaria Infections, THE ARCHIVES INT. MED., 1909, iii, 446.

The hemoglobin estimations were made with a Tallqvist scale. In making the differential counts 200 to 500 cells were counted.

From Table 3 it is evident that the blood-picture is not greatly affected in mild infections. The hemoglobin in non-infected students was but slightly higher than in infected ones. Although the average eosinophil count was somewhat higher in the infected than in the non-infected students, the eosinophils were not increased at all in many who harbored the parasites. In one spread counted, not one eosinophil was seen in counting 500 cells; some spreads from non-infected students showed from 4 to 8 per cent. and one 17 per cent. So while the presence of an eosinophilia should lead us to examine the stools, its absence should not influence us to neglect it.

TABLE 3.—Comparative Blood Findings in Sixty-six Cases of Intestinal Infection

Estimation.	Negatives.			Hookworm.			Trichuria.			Strongyloides intestinalis			Hymenolepis nana.		
	Highest.	Lowest.	Average.	Highest.	Lowest.	Average.	Highest.	Lowest.	Average.	Highest.	Lowest.	Average.	Highest.	Lowest.	Average.
Hemoglobin	100	80	95	100	80	92	90	85	87.5	90	80	84	90	85	89
Eosinophils	9.4	0.0	1.9	21.0	0.0	5.0	5.0	1.0	3.1	13.2	2.5	8.9	7.0	1.6	4.6

The above results demonstrate that hookworm infection is prevalent not only among the working classes and poor people, but also among the upper classes in infected districts; that in the country and smaller towns at least 30 per cent. of young adults between the ages of 15 and 25 are infected. Judging from the number who give a history of ground itch, a much larger proportion of people under this age harbor the parasite.

We wish to emphasize the value of the washing and centrifugalizing method of examination in detecting mild infections. Our results would indicate that two-thirds of the mild infections are overlooked in the ordinary stool examination.

We wish to thank Dr. W. C. Harkey, of Kansas City, Mo., for his assistance in part of this work.

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THE ANIMAL PARASITES FOUND IN THE INTESTINES OF NATIVE CHILDREN IN THE PHILIPPINE ISLANDS.

By Isaac W. Brewer, M. D.,
Camp Connell, Samar, P. I.

(Published under the imprimatur of the American Society of Tropical Medicine.)

The animal parasites which inhabit the intestines are one of the most important factors in the pathology of the tropics.

In the Philippine Islands the number of persons who harbor these parasites is very great. Garrison (1) examined 4,106 inmates of Bilibid Prison and found eighty-four per cent. infected. Later, in conjunction with Llamas (2), he examined 389 women and children in Manila of whom eighty-nine per cent. were infected. In the medical survey of the town of Taytay (3) 1,000 persons of all ages were examined, 95.9 per cent. being infected.

So far as is known no one has made an especial study of the parasites found in children in these islands. Having in mind the great mortality amongst Filipino children and the gratifying results obtained by ridding the inmates of Bilibid of these unwelcome guests, I started out to examine the fæces of all the children of the town of Danao, which is situated on the east coast of the Island of Cebu about twenty miles north of the town of Cebu. Owing to a change of station the work had to be terminated when but fifty-one children had been examined. The results of this study are presented as a preliminary contribution to the question and as an addition to the geographical distribution of the parasites in the islands.

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Of the fifty-one persons examined forty-seven or 92.2 per cent. were infected. The infections with each parasite were as follows:

	Cases.	Percentage.
Ascaris lumbricoides,	38	76.4.
Trichuris trichiura,	26	51.0.
Hookworm,	18	35.3.
Cestodes,	3	5.9.
Amœbæ.	3	5.9.

In one case the *Balantidium coli* was found and in another *Strongyloides intestinalis.*

Twenty-eight of the children were males and twenty-six were females, and one only was over nine years of age. None of these children complained of being sick nor did any appear to be unwell. However, one case, a boy of fourteen years, was treated for an ascaris infection and twenty-nine worms were recovered, after which his fæces remained free from ova. He gained very much in weight and was much more energetic than before the treatment.

Of the eighteen cases infected with hookworm none appeared to be sick although some of the infections, judging from the number of ova in the stools, were heavy. Apparently this worm does not cause the same amount of disability that it does in Puerto Rico and the southern portion of the United States.

Combining the Taytay and Danao cases we have 404 children under fifteen years of age, 368 or 91.9 per cent. of whom were infected. The infections with the several parasites are as follows:

Ascaris lumbricoides,	82 per cent.
Trichuris trichiura,	68 per cent.
Hookworm,	8 per cent.
Amœbæ,	2 per cent.
Strongyloides intestinalis,	1 per cent.
Oxyuris vermicularis,	0.7 per cent.
Balantidium coli,	0.2 per cent.
Cestodes,	0.2 per cent.

The importance of ridding the children of these parasites can not be overestimated. While in many instances they cause no marked symptoms they, without doubt, are a factor in the malnutrition and poor development of many of the native children, and probably predispose them to dysentery, tuberculosis, and other diseases.

This has been demonstrated in Bilibid Prison, where the general death rate fell from seventy-five to twenty as soon as a systematic campaign against intestinal parasites was begun.

Physicians in the United States rarely consider animal parasites when treating children. Most of the test books on diseases of children, which are largely based upon hospital statistics derived from institutions in large cities, speak lightly of the animal parasites. However, during the past decade we have learned that the hookworm is of the greatest importance in the pathology of the southern States, and it is very probable that if the fæces of children in small towns and the rural communities are examined we will find that other parasites are much more common than is generally believed.

Stiles and Garrison (4) examined the fæces of 123 children of an orphan asylum in the District of Columbia and found 21.1 per cent. infected. *Trichuris trichiura* was found in 13.1 per cent., *Ascaris lumbricoides* in 4.8 per cent., *hymenolepis nana* in 4.8 per cent., and *Oxyuris vermicularis* and hookworm in 0.8 per cent. These statistics certainly should cause the careful practitioner to look more often for parasites in the stools of children.

REFERENCES.

1. *Philippine Journal of Science,* iii, Section B, p. 191.
2. *Ibidem,* iv, Section B, p. 185.
3. *Ibidem,* iv, Section B, p. 257.
4. *Bulletin No. 28 of the Hygienic Laboratory af the United States Public Health and Marine Hospital Service,* p. 18.

THE RELATION OF MOSQUITOES TO FILARIASIS IN THE REGION OF SAN FRANCISCO BAY*

CREIGHTON WELLMAN, M.D.
EDWARD VON ADELUNG, M.D.
AND
FINLEY M. EASTMAN
OAKLAND, CAL.

The constant presence of filariasis in the cities bordering San Francisco Bay has long rendered it desirable to know if the indigenous mosquitoes of this region are efficient hosts for the parasite at the temperature normally found in this part of California. In other words it is a desideratum to learn if an Oriental infected with filariæ residing, for instance, in Oakland might be a menace to the community in which he lives. With this object in mind we have undertaken some experiments.

REPORT OF EXPERIMENTS

The Source of the Filariæ.—A Japanese man, aged 29, was found on Dec. 10, 1909, to have sharp-tailed, sheathed filarial embryos in his night blood. This man came to San Francisco six years ago from Japan, stopping at Hawaii three months on the way. He went to Alaska four years ago and since his return to California has resided for three years in Oakland.

The Mosquitoes Used in the Experiments.—These were all bred from larvæ collected in rain-water barrels, etc., which on breeding out proved to be two common species already reported from this part of California, namely, *Culex consobrinus*

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* From the Laboratory of Tropical Medicine, Oakland College of Medicine.

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(Rob.-Desv.) and *C. tarsalis* (Coq.). The males soon died in captivity but the females were easily kept alive in gauze cages, protected from bright light and fed on fresh grapes, which they readily sucked.

Time and Manner of Feeding.—The patient's blood was first examined late at night and proved to contain microfilariæ in plenty, and the mosquitoes were then removed from the cage in glass tubes and wide mouthed bottles, care being taken not to injure the insects. These containers were inverted over the flexor surface of the patient's forearm. It was found that some of the mosquitoes fed very slowly, in several instances an hour elapsing between the time the tube was placed on the arm and the mosquito's beginning to suck blood. When the insects had fed to repletion they were transferred to a cage containing a dish of water and kept at the ordinary temperature of the laboratory with some protection from the light. On the seventh, fourteenth and twenty-first days, after feeding, part of the mosquitoes were dropped alive into 80 per cent. alcohol, an equal number of controls which had fed only on fruit being treated in the same manner each time, and the bottles carefully labeled. To prevent error, two lots of mosquitoes were fed and controlled after this method, the dates of the first feeding of the two lots being December, 1909, and January, 1910, respectively.

Technic Employed in Preparing the Mosquitoes.—This may be described under two heads, namely, (1) fixing and hardening of mosquitoes, and (2) staining and mounting.

Under the first head it will be remembered that the insects had been dropped alive in 80 per cent. alcohol. They were removed from this and the legs and wings cut off. Next they were placed in 95 per cent. ethyl alcohol for twenty-four hours. From this they were transferred to absolute alcohol for twenty-four hours. From absolute alcohol they were put in absolute alcohol and ether (equal parts) for twenty-four hours. From this mixture they were transferred to ether for twelve hours. From the ether they were placed in 3 per cent. celloidin for three days and afterward into 6 per cent. celloidin and placed in 80 per cent. alcohol to harden for twelve hours. The specimens were then sectioned and the sections kept in 80 per cent. alcohol previous to staining.

Under the second head we may record the following steps. The sections were taken from the alcohol and placed in tap-water to remove the alcohol. Next they were stained with Delafield's hematoxylin for two minutes and afterwards washed in tap-water to remove surplus of stain. Acid alcohol (95 per cent. ethyl alcohol with 1 per cent. hydrochloric acid) was used to differentiate the sections, the sections being placed for three minutes in this mixture. Next the specimens were placed in 95 per cent. alcohol for three minutes to dehydrate. The sections next were passed through beechwood creosote for five minutes to clear them and finally fixed on slides and mounted in xylol balsam under cover glasses.

Result of Examination.—No developmental forms or other extraneous bodies were seen in the thoracic muscles or any other part of the sectioned mosquitoes. The appearance of the mosquitoes fed on the patient's blood is identical with that of the mosquitoes used for controls. As the sections are thin and the staining good, and as Dr. Wellman is familiar with the appearance of developmental forms of filariæ there seems to be little room for mistake.

Conclusions.—We consider that we have shown by this experiment that the two commonest species of Culex mosquitoes in Oakland are not efficient hosts at room temperature for the nocturnal sheathed microfilariæ occurring in our Japanese patient. It is possibly not too much to say, in view of these findings, that there is probably little danger that Orientals who are infected with filariæ will infect the inhabitants of the San Francisco Bay cities under present conditions.

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A CASE OF INFECTION WITH BALANTIDIUM COLI.

By Isaac W. Brewer, M. D.,
Camp Connell, Samar, P. I.,

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Balantidium coli is quite common in hogs, but rarely infects human beings, and the symptoms caused by its presence in the human intestines have not been fully studied.

Strong and Musgrave, working in Manila, studied a number of cases of dysentery which they believed were caused by this parasite.

During the routine examination of the stools of children living in the town of Danao, Province of Cebu, Philippine Islands, the stool of O. E., aged five years, was brought to the laboratory. In appearance it did not differ from other stools which were examined daily, nor was there anything characteristic about the odor. Examination, with a 1/6 inch objective showed ova of *Ascaris lumbricoides*, *Trichuris trichiura,* and hookworm. A number of ciliates were also seen, which on closer examination proved to be a *Balantidium coli.* When first placed upon the slide it was very active, but later became less active.

The mother stated that the child had always been well, but for several days had had one or two loose movements of the bowels each afternoon. Other facts than this she could not remember that the child had ever had diarrhœa or dysentery. The

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little girl appeared to be well and was seen occasionally for two months during which time no sickness developed.

Circumstances over which I had no control prevented a more thorough study of the stools in this case. After finding the parasite in this case the fæces of a number of hogs was examined but in no instance was the parasite found.

A Case of Filarial Hematochyluria

TREATED AFTER THE METHOD OF WHERRY AND McDILL WITH APPARENT RECOVERY

CREIGHTON WELLMAN, B.A., M.D.

AND

EDWARD von ADELUNG, B.S., M.D.

OAKLAND, CAL.

A CASE OF FILARIAL HEMATOCHYLURIA

TREATED AFTER THE METHOD OF WHERRY AND MCDILL WITH APPARENT RECOVERY *

CREIGHTON WELLMAN, B.A., M.D.

AND

EDWARD von ADELUNG, B.S., M.D.

OAKLAND, CAL.

Numerous remedies have been tried in the treatment of filarial hematochyluria, and there is considerable literature on the subject. Lawrie,[1] in 1891, seemed to get good results from the administration of thymol, and Flint,[2] in 1895, thought he had a cure in methylene blue, but subsequent writers have failed to confirm their results. In 1905 Wherry and McDill[3] reported a case treated by thorough cinchonization and subsequent exposure to the x-rays.[4] We quote from their report as follows:

> She (the patient) was given 80 to 90 grains of quinin sulphate during forty-eight hours, followed by x-ray exposures of five minutes, with the tube 18 inches away. Quinin having been administered daily, these exposures (over the lumbar region) were performed at 2 to 3 p. m. on September 8, 10, 11, 12, 14, 16, 17, 18, and again after cinchonizing as before at 9 p. m. on September 29 and 30. On October 2 the skin over the chest and abdomen became reddened and hot. A chill and left

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* From the Laboratory of Tropical Medicine, Oakland College of Medicine, Oakland, Cal.

1. Lawrence: Lancet, London, Feb. 14, 1891, p. 364.

2. Flint: New York Med. Jour., June 15, 1895, p. 737.

3. Wherry and McDill: Jour. Infect. Dis., June 24, 1905, p. 412.

4. In a footnote the authors add: "Unfortunately we are unable to state the exact hardness of the x-ray bulbs. In order to obtain a clear radiograph of the bones of the pelvis with this apparatus (the one used) an exposure of fifteen minutes with the bulb at a distance of five inches from the skin is necessary. Filarial embryos in a thin layer of blood, collected after cinchonizing, exposed to the rays for five minutes with the bulb 16 inches away are not killed but they squirm about in a very excited manner.".

pleurisy developed. Paracentesis produced about 600 c.c. straw-colored fluid on October 8. Skin scarlet all over body. All this time the urine remained thick and bloody, but on October 10 became normal and has remained so. The temperature throughout, except during the attack of pleurisy, remained about normal, 97 to 99.4 in the morning and 98 to 99.4 in the evening. Until the pleuritic attack the patient had gained 25 per cent. in weight and general appearance, and although an evening temperature of 1 to 3 F. persisted until October 22, she regained her strength so rapidly that on October 29 and 30 the *x*-ray was again applied for fifteen minutes, after quinin, with the bulb five inches away. Although the patient has been at home and walking about for the last two months her chyluria has not returned. The living embryos still persist in her blood.

About four years later the authors report again as follows on the case:

The hematochyluria cleared up on Oct. 10, 1904. Two months later filarial embryos were still present in the peripheral blood, but repeated examinations since, made about once a year, have failed to reveal the embryos. The last examination was made one year ago, 1908. The patient is now in Nagasaki and said to be in good health.

The writers of the present paper wish to record a similar case treated with quinin and *x*-rays, resulting in apparent recovery. While it is too soon to say more than we have indicated in the title to this report, yet the recovery is up to the present date (Jan. 24, 1910) complete and so far may be regarded as a confirmation of Wherry and McDill's observation. The history of our case is as follows:[5]

Patient.—H. U., aged 26, single, Japanese, came to San Francisco six years ago from Japan, stopping at Hawaii three months on the way. He has been a resident of Oakland for three years; went to Alaska four years ago and on his return to California had hematochyluria for two months in August and September. In 1908 he had another attack which began in August and lasted up to the date when first seen by us (Dec. 14, 1909). He was not very strong but had no pain to speak of except a slight pain below right scapula on rising.

Examination.—The patient was a fairly well-nourished Japanese with no symptoms except the character of the urine and weakness. Pulse 100, temperature 98. An examination of his blood at midnight showed considerable numbers of a sheathed filarial embryo. The urine was almost as turbid as milk and had a decided bloody tinge. It was examined on

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[5] Wherry and McDill: Jour. Trop. Med. and Hyg., Aug. 16, 1909, p. 241.

December 12, with the following results: Specific gravity 1,028, reaction slightly acid, albumin about 0.3, no sugar, no fat. A differential leucocyte count on the same date revealed the following findings:

Polymorphonuclear neutrophiles	46 per cent
Lymphocytes	29 per cent
Large hyaline mononuclears	14 per cent
Eosinophils	11 per cent

Transitionals counted with polymorphonuclears.

Treatment.—The patient was put on the treatment suggested by Wherry and McDill. We give the details of the treatment, as these are important in a purely empirical question like the present in which we have no idea of the principles involved.

The quinin was given as follows: December 27, 6 a. m., one capsule,[6] 10:30 a. m. two capsules.

December 28, 2 a. m., 2 capsules; 6 a. m., 2 capsules; 9:30 a. m., 2 capsules; 1 p. m., 2 capsules; 4:30 p. m., 2 capsules; 8 p. m., 2 capsules.

December 29, 1:15 a. m., 2 capsules; 7 a. m., 2 capsules, 10:25 a. m., 2 capsules; 1:30 p. m., 2 capsules; 4:45 p. m., 2 capsules; 8 p. m., 2 capsules; 11:20 p. m., 2 capsules.

December 30, 2:30 a. m., 2 capsules; 5:45 a. m., 2 capsules; 9 a. m., 2 capsules; 12:30 p. m., 2 capsules; 3:35 p. m., 2 capsules; 7 p. m., 2 capsules; 10:15 p. m., 2 capsules.

December 31, 1:45 a. m., 2 capsules; 5:15 a. m., 2 capsules; 9 a. m., 2 capsules; 1 p. m., 2 capsules; 6 p. m., 2 capsules; 11 p. m., 2 capsules.

Jan. 1, 1910, 4 a. m., 2 capsules; 8 a. m., 2 capsules; 12 p. m., 2 capsules; 5 p. m., 2 capsules; 9 p. m., 2 capsules.

January 2, 1:30 a. m., 2 capsules; 5:30 a. m., 2 capsules; 9:30 a. m., 2 capsules; 1 p. m., 2 capsules; 6:30 p. m., 2 capsules; 10 p. m., 2 capsules.

January 3, 1:30 a. m., 2 capsules; 11 a. m., 2 capsules; 2:30 p. m., 2 capsules.

January 4, 9 a. m., 2 capsules; 12:45, 2 capsules; 4:30 p. m., 2 capsules; 8 p. m., 2 capsules; 11 p. m., 2 capsules.

January 5, 7 a. m., 2 capsules; 10:30 a. m., 2 capsules; 2 p. m., 2 capsules; 5:30 p. m., 2 capsules; 9 p. m., 2 capsules.

January 6, 1 a. m., 2 capsules; 6 a. m., 11:30 a. m., 2 capsules; 3:30 p. m., 2 capsules; 7 p. m., 2 capsules.

January 7, 2 capsules; 7 a. m., 2 capsules; 11 a. m., 2 capsules.

From this on to Jan. 12, 1910, the patient took three capsules per day.

The patient complained considerably of the symptoms of cinchonism at first and was with some difficulty persuaded to continue the quinin.

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[6] Each capsule contained five grains of quinin sulphate.

The *x*-ray exposures were given as follows:[7] December 14, one and a quarter minute exposure.

December 22, one minute exposure.

December 31, one minute.

January 7, forty-five seconds.

January 12, thirty seconds.

The report of the patient was as follows: December 28, 29, 30, he suffered considerably from the quinin and was very weak.

December 31, patient felt weak but improved.

January 3, he felt stronger.

January 7, he felt stronger than he had felt for a long time; was losing in weight; weighed 126 pounds, the last time he had been weighed previously; now weighed 115½ pounds, in the same clothing.

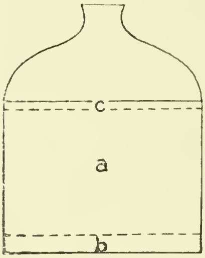

Fig. 1.—Gross appearance of solids in urine after standing (before treatment); a, amber color; b, blood, etc.; c, "cream."

January 11, he felt better; had gained slightly in weight.

January 12, he felt and looked much better.

The report on the urine now follows: December 8, reddish milky, reaction acid; albumin present by heat and acid tests, no sugar.

December 12, as above.

December 22, urine the same. On standing several days it appeared as shown in Figure 1.

December 27, urine was much clearer; no white upper layer, lower layer much less, a markedly improved urine. Red and white corpuscles present, also epithelium, no casts.

December 31, urine was clear amber; no albumin by heat or acid test. It had been clear nearly four days.

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[7] Twelve-inch coil; direct current; Wehnelt interrupter; 6¾-inch bulbs (Friedlander and Gundlach); distance from target *to table-top,* 15 inches; 3-inch vacuum which sometimes ran up to 6 or 7 inches during treatment.

January 3, urine was perfectly clear , pale amber, had been clear for a week. It had never been clear before since the patient's illness began in 1908.

January 7, urine was still clear; color pale amber; no albumin by heat or acid test.

January 12, urine had slight trace of albumin, reaction acid (Fig. 2).

January 14, urine was perfectly clear; no albumin.

The blood findings were also of interest. The number of microfilariæ in the peripheral circulation was not large even when the patient was first seen. The chart (Fig. 2) shows the comparative number of embryos found in equal sized drops of blood on the dates mentioned. The blood was always taken at night as with one exception (when a single embryo was found after a long search) the filariæ were absent from the blood taken in the day time.

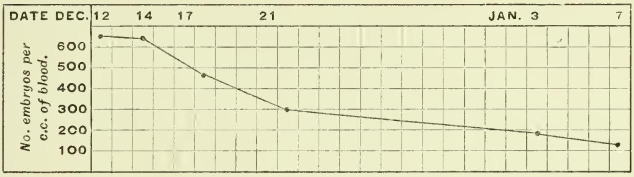

Fig. 2.—Chart showing the comparative numbers of microfilariæ in the peripheral blood at different times during the treatment.

The differential leucocyte count of Dec. 12, 1909, has already been given. On Jan. 7, 1910, the blood gave the following count:

Polymorphonuclear neutrophils	40 per cent
Lymphocytes	39 per cent
Large hyaline mononuclears	13 per cent
Eosinophils	8 per cent

Transitionals counted with polymorphonuclears.

On January 12 the embryos still persisted in the blood (taken at 2:30 a. m.) but in very small numbers, only one being found in 2 slides. No attempt was made to estimate their number per cubic centimeter. It should be said that the embryos were never found in the centrifugalized urine.

At the present writing (Jan. 24, 1910) the patient is very happy and encouraged and looks like a different man.[8]

In conclusion some of the interesting points connected with this case are as follows:

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[8] An embryo was found after some search in his blood on the night of Jan. 24, 1910, so the microfilariæ still persist in reduced numbers. The urine is still perfectly normal. We hope to report on the case again at some future time.

1. The apparent confirmation of the value of this method of treating filarial hematochyluria.

2. The absence of embryos from the urine even when the case was first seen.

3. The rapid decrease but persistence of a certain number of the microfilariæ in the peripheral night blood during the treatment.

Only time can settle the question as to the permanence of the cure, and we hope that other observers will test our results. We have tried in vain to find another case before publishing these notes, but, failing this, have thought that the suggestions arising from our experience warranted our laying the account of the experiment before other workers.

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CONJUNCTIVAL INFECTION IN MANILA.*

RALPH T. EDWARDS, M. D.,

DIRECTOR OF THE GOVERNMENT SERUM LABORATORY, PHRAPATOOM, SIAM.

The work upon which this paper is founded was done during the months of January and February, 1908, while in the service of the Bureau of Science, Manila, at which time conjunctivitis was prevalent among the prisoners at Bilibib Prison, where my daily routine was the necessary pathological and microscopic work.

Through the kindness of Dr. Shattuck, in charge of the hospital and sanitation work of the prison, and Dr. Christiansen, who was fighting eye infections among the prisoners, I was permitted to make slides and cultures from 22 of the 25 cases in the accompanying table.

In this paper we have made the diagnosis of Koch-Weeks conjunctivitis in all cases where the cultures gave characteristic bacilli, even when we were not able to make the diagnosis from the smear. Also we have left "undetermined" all cases in which we have failed in the culture.

In Nos. 5, 6, 7, the first culture was made in acid media, because no alkaline media was at hand, but transfer was made to alkaline media in two hours, therefore, in those cases, while the cause must have been B. Koch-Weeks or some other organism easily killed by acid, we have left the cases undetermined.

In No. 18, there was a luxuriant growth of micrococcus luteus (Kohn), but we do not think that it was the cause of the inflammation, but that probably the real offender was overshadowed by the luxuriant growth of the saprophyte, hence we consider that case also as undetermined

In all, 21 cases of conjunctivitis were examined. Out of this number, B. Koch-Weeks was isolated (9) times or about 42.90%; Staphylococcus pyogenes (aureus) alone, (2) times

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*Read before the American Society of Tropical Medicine, April 10, 1909.

No.	Discharge		Conj. red	Pain	Smear showed	Stain used	Culture	Remarks.
	Pus	Serum						
1	—	+	+	Slight	Not made	—	B. Koch-Weeks	....
2	+	+	+	+	Bacilli intra- and extra-cellular.............	Dilute C. F.	B. Koch-Weeks	....
3	—	+	+	+	Baclli seen, not seen intra-cellular........	" "	Staphylococcus pyogenes aureus	....
4	—	+	+	Slight	Small bacilli, no cells..	" "	—	Acid media
5	—	+	+	Slight	Bacilli seen, but not intra-cellular........	" "	B. Koch-Weeks	....
6	—	+	+	Slight	Negative.............	" "	—	Acid media
7	—	+	+	+	Bacilli seen, but not intra-cellular........	" "	—	Acid media
8	+	+	+	+	Negative.............	" "	—	....
9	+	+	+	+	Bacilli seen, but not intra-cellular........	" "	Staphylococcus pyogenes albus	....
10	+	+	+	+	Bacilli seen, but not intra-cellular-.......	" "	B. Koch-Weeks	....
11	+	+	+	+	Bacilli intra- and extra-cellular............	" "	B. Koch-Weeks	....
12	—	+	Slight	Slight	Small bacilli, no cells..	" "	—	....
13	—	+	+	Slight	Negative.............	Giemsa	B. Koch-Weeks	....
14	—	—	Slight	Slight	Negative.............	Giemsa	—	....
15	—	+	+	Slight	Negative (lost)........	—	B. Koch-Weeks	....
16	+	+	+	+	Cells only............	Dilute C. F.	Staphylococcus pyogenes aureus albus also	....
17	+	+	+	Slight	Intra- and extra-cellular bacilli...........	Dilute C. F.	B. Koch-Weeks	....
18	—	+	+	Slight	Cocci.	Methyl. blue	Micrococcus luteus (Kohn)	....
19	+	+	+	Slight	Bacilli intra- and extra-cellular............	King's stain	—	....
20	—	+	+	+	Negative.............	" "	B. Koch-Weeks	....
21	+	+	+	+	Bacilli intra- and extra-cellular.	" "	Staphylococcus pyogenes aureus	....

No.	Trachoma case	Diagnosed by	Smear	Stain	Culture
22	Trachoma case	Dr. Christiansen	Negative	Giemsa, King's, Dilute C. F.	B. trachus
23	Trachoma case	Dr. Christiansen	Negative	Giemsa, King's, Dilute C. F.	Negative
24	Trachoma case	Dr. Stafford	Negative	Giemsa, King's, Dilute C. F.	Aspergillus flavus
25	Trachoma case	Author	Negative	Giemsa, King's, Dilute C. F.	Negative

or about 9.86%; Staphylococcus pyogenes with albus (1) time or about 4.43%; Staphylococcus albus alone (1) time or about 4.43%; Micrococcus luteus (Kohn) (1) time or about 4.43%; negative stain and culture (3) times or about 13.30%; smear apparently positive but culture negative (6) times or about 26.60%.

In case (24), we thank Dr. Stafford, Chief of the Philippine Civil Hospital, for the courtesy of allowing us to take cultures both before and after the operation for trachoma. While in this case the culture showed aspergillus flavus, we do not think that so common a fungus could be the cause of trachoma, but that its presence was only accidental.

From No. 22, B. trachus, *nov. spec.*, 1909, was isolated, but on account of lack of evidence, we do not claim it as the cause of trachoma but publish this as a help to any one who can carry the work farther, and prove it harmless or pathogenic as the case may be.

Since many have failed in the effort to cultivate the cause of trachoma, it seemed best to use special media. The Koch-Weeks bacillus grows best on 5% peptone alkaline agar; the gonococcus grows best in the presence of hydrocoele fluid or some similar body exudate. With these two things in mind we decided to try media in which B. Koch-Weeks grows best after having added a drop or two of blood from the ear of the patient from whose eye the culture was taken. This blood we secured sterile on a platinum loop and smeared over the surface of the agar. Cultures made on acid media were sterile as were also those made without the addition of the fresh blood. Later rabbit blood was tried with as good success as human blood, but clear serum and exudates were not tried.

B. trachus is a small polymorphous organism about 1 in. long and generally about 1/3 as broad as long, without spores, or granules, non-motile, stains poorly with methylene blue, but well with dilute carbol-fuchsin, Wright-Romanowsky and King's stains. It grows slowly on 5% peptone alkaline (blood-smeared) agar in small white colonies, which become visible to the eye on the second day and reach their maximum size (about 1 mm.) in 5 or 6 days.

It remains alive on such media for at least a month, but if planted on 5% peptone alkaline agar does not appear to grow at all, yet lives in this condition for at least (10) days as may be seen by adding fresh blood when the colonies appear after two days.

No positive results were obtained by animal inoculation; the conjunctivae of rabbit, guinea-pig and monkey (Macacus philippinensis) showing no change a month after inoculation.

There has been a report of successful inoculation upon the conjunctiva of higher apes, but there were none of these to be had, and we did not think human experimentation justifiable. Therefore the pathogenicity of this organism is still unsettled.

There is little chance for reference to literature, here, therefore other authors will please pardon me for not giving exact references as all such reference must be done from memory.

Gov't. Serum Laboratory, Phrapatoom, Siam.

TUBERCULOSIS IN THE PHILIPPINE ISLANDS

BY

ISAAC W. BREWER, M. D.

Published Under the Imprimatur of the American Society of Tropical Medicine

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TUBERCULOSIS IN THE PHILIPPINE ISLANDS

Published Under the Imprimatur of the American Society of Tropical Medicine

BY ISAAC W. BREWER, M. D.

Tuberculosis has been called the universal disease because it prevails in all portions of the world. However, it is rarely considered in thinking of the diseases of tropical countries. Osler says* "The disease (tuberculosis) is perhaps more prevalent in the temperate regions than in the tropics." Probably this is the opinion held by most persons who have not lived in the torrid zone.

In the Philippines tuberculosis is one of the greatest causes of death. From the medical survey of the town of Taytay, Nichols came to the conclusion that one per cent. of the inhabitants had tuberculosis. The statistics for thirty provinces for the year 1907, representing a population of over four million persons, show a death rate of 210.9 per 100,000. This is surely less than the real rate, for only well marked cases of phthisis are so recorded by the town secretary, a layman, who issues the death certificates.

Table I shows the death rate in the Philippine Islands for the year 1907 in comparison with the rates in other countries.

TABLE I

Death rate per 100,000, from pulmonary tuberculosis:

County.	Rate.
Ireland	218.5
Philippine Islands, excluding Manila, 1907	210.9
Norway	200.4
Switzerland	190.7
Germany	181.9
United States, registration area	172.3
Scotland	150.1
Spain	144.3
The Netherlands	138.8
Belgium	127.7
England and Wales	125.7
Italy	117.0

Excepting for the Philippine Islands, the above statistics are for the five years from 1901 to 1905.

In Manila, where the vital statistics are much more accurate, there were, during the year 1908, 10.646 deaths from all causes. Of these, 1,240, or 11.7%, were due to tuberculosis, which gives a death rate of 554.2 per 100,000. During the five years ending with 1908 there were in Manila 5,373 deaths from pulmonary tuberculosis, a death rate of 485.3 per 100 000. During the same period there were 4,472 deaths from bronchitis, a death rate of 404 per 100,000. Without doubt some of these cases of bronchitis were either pneumonia or tuberculosis.

Table II shows the death rate from pulmonary tuberculosis in Manila and certain cities in the United States having approximately the same population. These data are for the year 1908.

TABLE II

	Death Rate.
Manila, P. I.	486.2
Indianapolis, Indiana	184.7
Louisville, Kentucky	183.6
Providence, Rhode Island	153.4
New York City, Borough of Queens	125.5
St. Paul, Minnesota	88.8

The statistics presented show that the mortality from tuberculosis in the Philippines, both in the provinces and in Manila, is greatly in excess of the rate in the United States.

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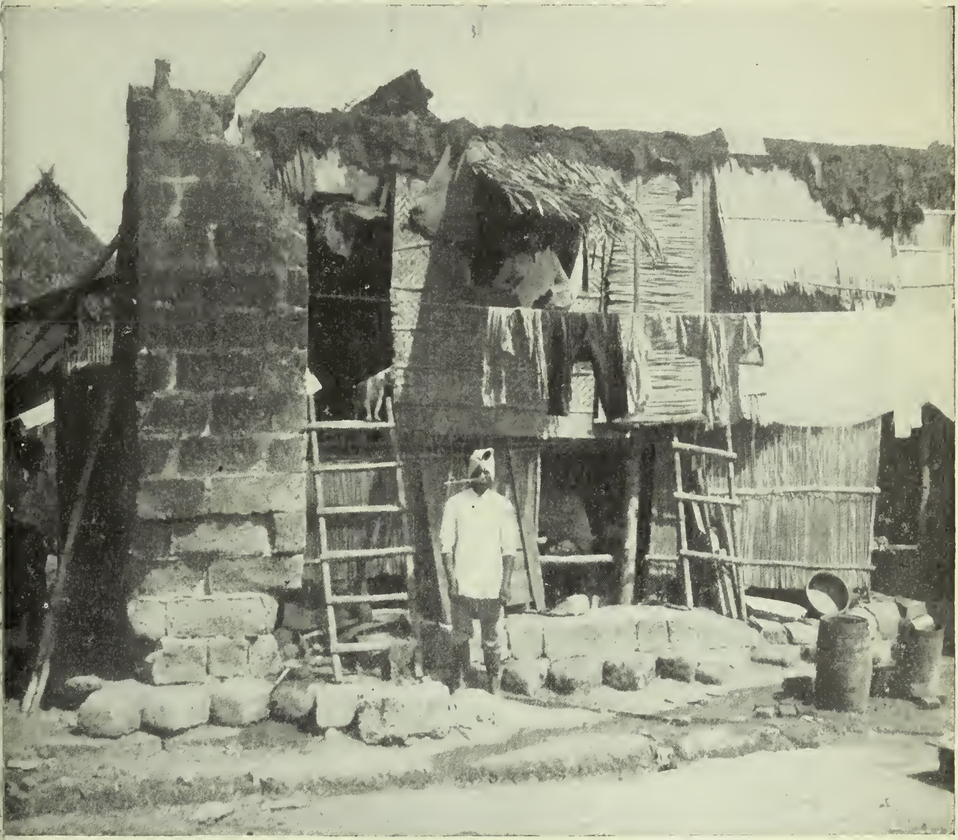
*Principles and Practice of Medicine, 6th Ed., p. 285.

is condition is far from satisfactory and is lly unnecessary. If there be any virtue in sh air and sunshine, there should be but y little tuberculosis in the Philippine Is- ds. The temperature rarely reaches 100 grees, and even in the cooler months the rmometer seldom registers fifty, except in mountains, where there is occasionally st and ice. In most portions of the Island is very dry from November to May, but rainy season varies according to the rela- n of the mountains to the prevailing winds. nerally, it is from June until November. ring this period it frequently rains for days a time and the relative humidity approxi- tes 100 per cent. However, the climate at is season is rarely so severe as to compel e to keep the house closed. In such a cli- te the inhabitants should obtain a maxi- um amount of fresh air, but the habits of the Filipino are such that fresh air is usually lacking in his residence.



NATIVE HOUSE IN THE SLUMS OF MANILA. TYPICAL OF CONDITIONS THROUGHOUT THE ISLANDS

According to Melvin, more than one per cent. of the beef cattle and two per cent. of the hogs that are examined by the United States Meat Inspectors are infected with tuberculosis. According to Gearhart* there were 60,000 hogs and 30,000 cattle killed in Manila abbatoir during the year 1909 and not one of those animals was found to have tuberculosis. The rarity of tuberculosis amongst hogs and cattle in the Philippines surely indicates that the climate in itself cannot be responsible for the great prevalence of the disease amongst the natives.

A study of the habits and surroundings of the natives of these Islands indicates that the great prevalence of tuberculosis is probably due to the following causes:

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*Bulletin of the Manila Medical Society, Vol. 1, No. 9, p. 4.

Bad hygienic surroundings.
Poor food.
Improper clothing.

The houses of the better class of natives, even in Manila, are lacking in ventilation and are religiously kept closed during the day to exclude the heat, and at night the windows are usually closed, because it is generally believed that the night air will cause fever. An actual count of two hundred houses in Manila, of all classes, made about midnight, showed that less than twenty-five per cent. of them had the windows opening on the street open. In many of the houses the open windows were apparently not in the bedroom. It is not uncommon to find horses and other animals kept in the lower floors of the best houses in Manila.

The poorer natives, both in the provinces and in Manila, live in thatched cottages. These seem to be very open and well ventilated, but on closer acquaintance it is found that the windows in them are also closed during the greater part of the day and all night. The space beneath the house is generally occupied by hogs, goats or cattle, and beneath the kitchen is frequently a filthy hog-wallow, in which much of the liquid refuse of the house is thrown. Chimneys are practically unknown and the smoke from the kitchen fire circulates through the house polluting the air. At night, a smoky lamp aids in polluting the air.

The Filipino is a great chewer and spitter. He expectorates wherever and whenever most convenient. If in a house, he spits out of the window but as often uses a crack in the floor, and the walls and the floor are generally soiled with his expectorations. Those who have tuberculosis enjoy the same privileges as to spitting as do the well. The habit of exchanging partially smoked cigarettes and cigars, which is very common, undoubtedly tends to spread the disease.

Over 90% of the native inhabitants are the hosts of intestinal animal parasites. Investigations conducted in Bilibid Prison have shown that while in many instances these unwelcome guests cause no symptoms in themselves they predispose their host to other infections, and the combination of an animal parasitic intestinal infection with a disease like tuberculosis hastens the fatal termination.

The average native seems to be poorly nourished. His diet consists of rice and fish, with a few roots, fruits and green vegetables. Occasionally pork, and more rarely beef, is included in the diet. Much of the food is poor in quality, especially the fish, which is cured in the sun, and from the odor about the place where it is dried much of it mu be partially decomposed.

Cotton cloth is generally used for clothin and it answers very well if kept dry, but du ing the rainy season it is generally damp an shivering natives are a common sight at suc times.

The United States has an immense sanitar problem to solve in the Philippine Islands, an one that will take years, hard work and tac Not the smallest portion of this problem the eradication of tuberculosis. To accomplish this, an active campaign of educatio must be instituted, but the methods adopt must differ from those used in other countrie because these people are not so far advance in the study of hygiene. It is doubted if the have reached a point where sanatoria woul be of much service, but they will readily ava themselves of the facilities offered by a loc dispensary or hospital, and the more of suc institutions the Americans establish in th small country towns the better will be th results of the campaign.

Excepting in the larger towns, there is great lack of medical attention. The nativ has so little money that few towns could support a physician, unless he devoted his energie to some other occupation and made medicin a side issue. The Island of Cebú has a population of over six hundred thousand and density of population of 337 persons to th square mile, and as far as I can learn ther are no physicians in that province, exceptin in the town of Cebú.

The Bureau of Health is attacking th problem as best it can with the funds avai able, but the resources of the Insular Treas ury are taxed almost to the limit, and th Bureau of Health has to expend much of it appropriation in the suppression of smallpox cholera, and in endeavoring to improve th sanitary conditions of the Islands in genera In money, the Philippine Islands are poo Municipal dispensaries and hospitals are ou of the question, excepting in the largest c the towns. If the Philippines are to b brought into line with the rest of the worl in the warfare against tuberculosis, they wi have to have help from the philanthropic cit zens of the United States. There could b no better charity than the support of a san tary mission in one of the provincial town An enthusiastic physician, with a few traine nurses and a good supply of drugs, could accomplish wonders in these Islands. A fe such missions have been established and ar doing as much work as possible with the limited funds. There is room for many mor and it is hoped that the citizens of the Unite States, who have ever been willing to sen money to foreign countries to enlighten th heathen, will turn some of their charity t our colonies in the Philippine Islands.

DISEASES IN THE TROPICS.*

Four Lectures.

By CREIGHTON WELLMAN, M. D.,

Professor of Tropical Medicine in the Oakland College of Medicine, American Secretary of the Society of Tropical Medicine and Hygiene, Late Medical Officer, Bihe, Province of Angola, Portuguese West Africa.
(From the Laboratory of Tropical Medicine, Oakland College of Medicine.)

Lecture I. Insects and Human Disease in the Tropics.
Lecture II. The Diseases of Portuguese West Africa.
Lecture III. Why the Physician in Temperate Climates Should Study Tropical Diseases.
Lecture IV. The Health Problems for Caucasians in Tropical Colonization.

Prefatory Note.

The following addresses constitute part of a series of lectures first prepared and delivered at the University of Nebraska on invitation of Professor Henry B. Ward, late Dean of the medical school of that university. While presented in the first instance before the medical and general science faculties and students of the University of Nebraska at Omaha and Lincoln (the last lecture of the series being before a special university convocation), other requests led to similar groups of talks before various other universities and scientific bodies. The substance of two medical and two popular lectures of the series is now printed, consisting largely of the original notes or abstracts of the addresses actually given to which have been added passages from stenographic reports. The author hopes that tropical men in reading over the following pages will keep in mind the circumstances of their delivery and their distinctly occasional character, as none of the lectures were prepared for an audience of tropical experts or even for one composed entirely of medical men. The general aim has been rather to stimulate interest, both within and without the medical profession, in the important subject with which they attempt briefly to deal.

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* Published under the Imprimatur of the American Society of Tropical Medicine

LECTURE I.

Insects and Human Disease in the Tropics.

I cannot better begin this lecture than by relating that Sir Lauder Brunton once made the remark in an address before the London School of Tropical Medicine that ''the study of tropical diseases is becoming to a great extent identified with the study of the insects which transmit them." I conceive that no line of medical and biological research is more interesting or significant to-day than investigation in the rapidly widening field indicated in the title of the present lecture. But it is of prime importance that the man coming to such research should bring with him an adequate training in the biological sciences. I can think of no phrase more fitting to emphasize this point than a quotation from Sir Patrick Manson who has remarked that ''The student of medicine must be a naturalist before he can hope to become a scientific epidemiologist or pathologist or a capable practitioner.'' Not only is it discouraging to stand before medical students who lack the broad foundation in biology to enable them to correlate and appraise much of the data which teachers lay before them, but even in the ranks of our profession there obtains too little realization of Sir Patrick's remark. It is humiliating for instance to see an audience of zoologists smile at the utterances of even some of our distinguished medical men when the latter venture on subjects touching the bionomics or systematics of organisims other than the human species. While indexing the literature which deals with the subject of this lecture in the Army Medical Museum in Washington, D. C., I found that hundreds of papers with good clinical and pathological data were useless for my purpose because the species, genus or even family of arthropods discussed are not given, or given so carelessly as to preclude any sort of accuracy in citation. Some bionomic or systematic treatment of one or more groups of organisms ought to be given every medical student as an integral part of his medical training, particularly if he contemplate research work of any sort. No more fascinating field could be suggested in this connection than a study of any one of the important arthropod groups which subserve human disease in the tropics. It is in the hope of increasing any interest already existing in this important subject that I have ventured to address you on this occasion.

My remarks do not profess to be an exhaustive discussion of the subject announced. I shall attempt only to illustrate the principles involved in its study by referring briefly to a few typical species of insects *(sensu latiore)*, and shall confine myself largely to those forms which I have studied at first hand in West Africa. I should also add that when we speak here of insects of pathological interest not only are meant those species which disseminate pathogenic bacteria or protozoa, but also all those which give rise to pain or discomfort in man.

Taking up first the Arachnida we will glance at the mites, ticks, spiders, scorpions, etc.

Mites.—The itch mite has been well studied and is familiar to pathologists. All the cases of the so-called tropical disease known as Craw-Craw which fell under my notice in West Africa were found to be scabies, some of the cases, however, being almost incredibly severe and neglected. When last in Europe I was shown a case of "Craw-Craw" from the lesions of which certain constant, oval, homogenous bodies staining deeply with basic stains had been observed under the microscope. By means of a hand lens and needle I was able to demonstrate *Sarcoptes scabei* and then by obtaining and staining the feces from the mites to show that these were the supposed spores of fungi which had been predicated as the cause of the disease.

The so-called harvest mite or red bug *(Leptus* spp.), is well known to European and American authors. I found one species of these larval Trombidiidae in Africa, but was unsuccessful in my attempts to determine the adult. I have in my collection a number of other West African mites, chiefly Gamasidae and Tarsonemidae, which are parasitic, either on insects or higher animals. In America we have various species of these creatures, such as *Trombidium tlalsahuate* and *Tetranychus molestissimus*, which would repay further study.

Ticks.—A study of the ticks of West Africa throws much light on the general subject of tick-carried diseases. Perhaps the most common species throughout the colony are *Ornithodoros moubata, Amblyomma hebraeum* (which bites human beings, both in its immature and adult stages, and leaves a most painful wheal), *Boophilus decoloratus* and *Rhipicephalus coriaceus* (a new form possibly peculiar to the district). The first of these, *O. moubata,* is the only form actually convicted of causing disease there, although some of the others are interesting because they bite man and cattle. *O. moubata,* which was first described by Murray as "oblong, coriaceous, coloured something like a shark's skin, or slate colour, speckled with white spots or granulations all over it," is a veritable pest and infests the camps and huts of the natives in great numbers. I have found as many as a hundred in an hour in an old native hut. Their habits and method of biting are something like the bed bug's. In addition to being disgusting vermin they are the disseminators of *Spirochaeta duttoni* the cause of African relapsing fever. This spirochete is transmitted from man to man not only through the bite of the adult ticks, but the spirochetes are able to pass into the eggs and larvæ so as to enable the mature ticks of the succeeding generation to be infective. By using hammocks and wrapping the suspending ropes with a band of cotton wool dusted with insect powder we were able in Angola to control and stamp out a small epidemic of tick fever among coolies.

I also found that under some circumsances the embryos of *Filaria perstans* develop to a certain point in this species of tick. Whether or not it is an entirely efficient host and the carrier of *Perstans* filarias is still an open question.

It has been suggested that ticks are the transmitters of blackwater fever (which is suspected by some to be a piroplasmosis analogous to the red-water fever of cattle), yaws, leprosy and other diseases, but of these we cannot speak here.

American ticks well worth careful investigation and closely relate to *O. moubata* are *Argas persicus, Ornithodoros turicata, O.*

talaje, O. megnini, etc. The spotted fever of the Rocky Mountains is an interesting tick-carried infection recently proven by Ricketts to be transmitted by one of our indigenous species (*Dermacentor occidentalis*).

Spiders.—In West Africa I found some of the large species of *Nephila* or round bodied spiders (*N. senegalensis, N. pilipes,* etc), to be feared by the natives. In America we have the tarantulas (these differ among other features from other spiders by the fact that their mandibles work vertically instead of horizontally) which bite severely.

Scorpions.—The scorpions of Angola are justly avoided. The two commonest species in my collection are *Uroplectes occidentalis* and *Parabuthus afer.* The sting of the latter is sometimes a serious matter. The scorpions of other parts of Africa (*e. g. Androctonus funestus*) are even more formidable.

A common species in the southwestern part of our own country is *Buthus carolinianus,* but its bite is not serious.

Linguatulidæ.—These are Arachnoid parasites, and one genus *(Porocephalus)* occurs in Africa, although I have neve rseen a case.

Myriapods.—I must mention the Centipedes. The larger of these creatures bite savagely. In West Africa we have *Scolopendra morsitans* and several species of *Cormocephalus,* all of which do not bear handling with impunity. The effects of their bite seem to be somewhat more severe than the stings of large Hymenoptera. Among the Millipedes I may appropriately mention two genera of African Julidæ, namely, *Spirostreptus* and *Odontopyge.* These are greatly feared on acount of the intense smarting and burning which they leave in their wake if they crawl over the body of man. The track looks like a burn from a hot iron drawn across the skin. The poisonous secretion is probably from the *foramina repugnatoria* which are at the sides of the segments and look like tracheal stigmata. The real stigmata are on the ventral surface of the segments and are so minute as to be easily overlooked. I have recently learned with interest that Woolley and Wherry have confirmed the above statements by observing the Millipedes of India and Siam.

Myriapods have been mentioned among the hosts of tape worms (*Hymenolepis nana*).

We may now take up the insects proper, at the main groups of which we will glance.

Orthoptera.—It will surprise some of my hearers when I mention this order as of possible pathogenic importance. In doing this I do not refer to the fact that various Orthoptera serve as intermediate hosts of organisms inimical to man. The Gordiacea (of which there are some forty or fifty reported cases of pseudoparasitism in man) develop often in these insects. The suggestion has been made that the germ of beri-beri may be dependent for its development on cockroaches. A tape worm (*Davainea*) is also thought to be disseminated by cockroaches. But I would like to call especial attention to a giant earwig which represents a new genus and species and which has recently been described under the name *Dacnodes wellmani*. This powerful insect, which is from an inch to an inch and a half long, is capable of drawing a large drop of blood with its pincers, and as it lives in refuse heaps it has earned the name among the natives of West Africa of causing severe results (doubtless due to the introduction of septic matter under the skin of the victim) by its "bite". I was at first disposed to view this idea with suspicion but Commander Walker, R. N., has pointed out since that another giant earwig (*Anisolabis colossea* from Australia) has similar habits and enjoys a similar evil reputation. Another member of this last genus *(A. annulipes)* is said to harbor a cestode *(Hymenolepis diminuta)*.

Before leaving the Orthoptera I should not omit to mention that one member of this group *(Hemimerus talpoides)* is a true parasite on the large West African rat (*Cricetomys gambiense*), and it is therefore not impossible that a similar insect may eventually turn out to subserve directly some mammalian disease.

Bugs.—This group is one of the largest and most important of insect pests. The bedbugs, of which there are several species, are of great significance in connection with the spread of relapsing fever, Leishmaniasis, and doubtless of other affections. Captain Patton has written me some ineresting facts regarding the distribution of the various species of the genus *Cimex* in India, and I found also that the "bed bug" of Portuguese West Africa was not *C. lectularius* as has been supposed, but an entirely different species. My specimens are now in the hands of a specialist and will probably prove to represent a new form. The suggestion that plague is directly transmitted from man to man by bugs, as well as from rodents to man by fleas, while not yet confirmed, is interesting, as is the recent finding of acid-fast bacilli, probably lepra bacilli, in bugs in Hawaii. Lice, too, deserve attention. The dog tape worm is stated to be carried by a louse (*Trichodectes canis*). Daniels' ideas regarding lice and the spread of Beri-Beri deserve careful consideration. Observations on the lice of lower animals suggest the importance of a closer study of the human parasite. It may be worth while to mention here that while I found both the head and body louse among West African natives the crab louse *(Phthirius inguinalis)* was absent. Among other bugs the so-called "Kissing bugs," or Reduviidæ, deserve mention. One South American form *(Conorhinus renggeri),* is called "the Great Black Bug" of the Pampas and is mentioned by Darwin in his "Voyage of the Beagle." It sucks human blood with avidity. We have several species with interesting habits here in the United States. Among these are the masked wheel bug (*Opsicaetus personatus*), which preys on bed bugs and occasionally bites man, and *Prionotus cristatus,* which shares this habit. Perhaps the cone-nosed blood-sucking bug of the southwestern states (*Conorhinus sanguisugus*) is our most formidable species. The bite of this animal gives rise to severe effects which are reported in rare cases to cause serious symptoms lasting over months and even years and in some cases even to produce death. The descriptions of the effects set up by the insect point strongly to an infection of some sort, and reports from the tropics even more strongly suggest this. Of the various species with which I am familiar by far the most interesting is *Phonergates bicoloripes.* This bug I have proven to prey chiefly if not exclusively on *Ornithodoros moubata,* the tick which transmits relapsing fever and possibly filariasis and other diseases in West Africa. I have many notes on this bug's habit of mulcting these pathogenic ticks of their ingested blood. *P. bicoloripes* also bites man and gives rise to severe effects. The question at once comes up as to the possibility of a double cycle of development of some germ which may have been taken up originally by the biting bugs, ticks, etc., upon which the Reduviidæ prey, the latter in turn sucking the blood from the parasitic arthropods and allowing the organism to enter upon some yet unknown cycle of development, finally being possibly conferred upon a different host or even reinoculated into the same host. This may sound improbable but some of the very complex biological life cycles which have been demonstrated during recent years forbid our considering anything of this sort as impossible on *a priori* grounds.

Other groups of bugs, notably Lygaeidae also come to mind. Those of you who are interested in our tropical American bugs are recommended to look through the literature for reports on such species as *Rhodinus prolixus* from Colombia and Venezuela, *Arilus carinatus* from Brazil, etc., which are said to suck human blood.

Flies.—This group (including the fleas) is certainly the most significant of all from the view point of our lecture. There are two great divisions in the group, the first of which may be typified by the mosquitoes and the second by the common house fly, the fleas forming a closely allied but very specialized section.

We will first mention the genus *Phlebotomus,* one species of which (*P. Papatasii*) has within the last year been incriminated as the carrier of the "three-day fever" of Dalmatia, etc.

Without entering upon a detailed discussion of the mosquitoes I should not fail to state that the study of these insects is highly important, although the very chaotic condition in which the systematics of the family is unfortunately at present makes such a study very difficult.

In Portugese West Africa the most dangerous malaria carrier is *Myzomyia funesta.* I have found this species to show sporozoites in its salivary glands to the extent of 13 per cent of mosquitoes caught at random in one of the towns. In one military barracks I even found 23 per cent. *Pyretophorus austeni* is another of our dangerous forms. Of the culicines *Danielsia wellmani* and *Mansonia uniformis* may be mentioned as having to do with the spread of filariasis.

In America the malarial and yellow fever mosquitoes are of the greatest importance to the sanitarian and these are fortunately well known and easily determined species.

Before leaving this group of insects I should say that various other kinds bite man. The black flies *(Simulidæ)* are a pest in parts of this country. In Portugese West Africa one species *(Simulium wellmani)* is a veritable scourge, driving people from whole districts during part of the year.* Chironomidae (*Ceratopogon)* and the owl midges (Psychodidæ, *Phlebotmus)* also share these habits and are therefore deserving of study by the pathologist.

Coming now to the flies proper we may first mention the house fly. This pest is of such importance, not only in the tropics, but here in America, that its eradication deserves the co-operation of every citizen. The interesting researches of Grassi regarding the house fly as a carrier of the ova of intestinal worms deserve mention. The convincing work on the subject of the house fly and tuberculosis by Lord and others is of deep significance. The spectacle of flies going from virulent tubercular sputum to our food is not pleasant to meditate upon, and the persistence of viable bacteria in the feces of the flies is rather terrible to contemplate. The question of flies and typhoid fever is no less important. The number of cases of typhoid fever in many of the larger cities for last year was far too great for the population, and while money is constantly being expended for sewers and water supply, how much is being done to eradicate the house flies?**

It is not the house fly alone which is to be watched as a cause of human suffering and disease. Half a dozen other flies live in houses and act as disseminators of disease in much the same manner. The bottle flies and blow flies need mention. In tropical countries there are various species of *Chrysomyia, Dermatobia, Ochromyia,* etc., which invade the skin of man, their larvæ causing what is known as cutaneous myiasis. One American species, the so-called screw-worm (*Chrysomyia macellaria*), burrows in the deep tissues causing terrible lesions and even death. In some experiments carried out in goats I produced similar destructive myiasis with two species of West African flesh flies (*Sarcophaga africa* and *S. albofasciata*). Another fly observed was *Auchmeromyia luteola,* the larvæ of which do not invade the tissues but which have biting mouth parts something like a gadfly and suck blood in the manner of ticks and bugs. The possibility of such a creature carrying pathogenic bacteria or protozoa of course immediately occurs to one. Another of our West African species is *Cordylobia anthropophaga,* the larvæ of which ensconce themselves in the tissues as warble flies do in cattle. I have often squeezed these larvæ (which may give rise to boils and also severe ulcers) from the skin of man and other animals. This last species often occurs in babies and dogs in Angola. Another fly from that region and not heretofore convicted of causing myiasis is *Anthomyia desjardensii,* which I found in the intestines of a negress.

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* Austen. Illustrations of African Blood-Sucking Flies, p. 30.

** The principles of fly extermination are simple and easily understood, and the details are within the reach of any community. City ordinances regarding livery and boarding stables and other animal industries within the city limits should be passed and all animal excreta (in which the fly largely breeds) should be collected often and removed from the city or placed in dark fly-proof receptacles until it can be removed. Streets should be kept free from all horse excreta, and no dumping places should be allowed in or near a city. Such simple regulations as these (the infraction of which should be provided against by adequate penalties) would do much to lower the consumption and typhoid curve. The condition of slaughter-houses and manufactories should be rigidly inspected from the standpoint of breeding places of flies. The screening of houses and public buildings should not be neglected. The formula of a good sticky fly paper should be printed and distributed among the poor. Merchants who sell screens, traps, fly paper, etc., should be helped, in wording their advertisements, so as to catch the popular eye, and the newspapers should be made use of in educating the public to the need for protecting food from flies. Many other devices might be mentioned.

I cannot leave this discussion without speaking of the tse-tse flies. Those are muscid flies showing certain highly specialized characters and their study is of the greatest importance to those interested in the fate of the native Africans as well as of the big game and domestic cattle of their country. Eight different species are described and I am informed by Mr. Austen, our best authority, that specimens representing another species are in the British Museum collections. *Glossina palpalis* is the species concerned in the dissemination of sleeping sickness. In Portuguese West Africa a new subspecies (*Glossina palpalis wellmani*) takes the place of the typical form. The great secret of escaping infection with *Trypanosoma gambiense,* the flagellate protozoan which causes this terrible disease, is avoidance of the "fly belts." On one occasion by resurveying a road and running it 700 yards farther from the river bank, crossing a mile farther up stream and thus avoiding a fly belt, we were able in West

Africa entirely to avoid the introduction of new infections into a large and populous district.

Tabanidæ or gadflies are another important group which has been too little studied. One species has been shown to carry the trypanosomiasis of camels in Algeria, others are suspected of subtending *Filaria loa* and the family might well be investigated further. In Angola many species, especially *Tabanus wellmani* and *chrysops wellmani,* with numerous members of the genus *Haematopota* (mostly new to science) bite man severely and greedily. There are other flies which are as worthy of mention as those we have chosen, some of the most interesting belonging to Tropical America.

Fleas.—These animals have assumed great importance not only from the fact that they have been proven to transmit parasites of lower animals, but especially since bubonic plague has been found to be carried by them from rodents, in which it is endemic, to man. So much has been written on this subject and the leading facts are so well known that I do not need to enter into any exposition of them at this time.

In West Africa I found that of the many species (some of them new), which I collected, two *(Lemnopsyllus cheopis* and *Pulex irritans)* are among the most common in dwellings. Curiously enough, plague has never in historical times visited that part of the world, although there is an endemic focus of the disease, discovered by Robert Koch, in East Africa.

Perhaps the most interesting of all fleas is the very abundant and ubiquitous form known in Africa as the "Chigger" (*Sarcopsylla penetrans*). This strange animal was brought to Angola about thirty-five years ago by Portuguese from South America, spread right across the continent and is steadily making its way around the world, having already been reported from India and even Cochin China, where it has doubtless been carried by coolies returning from East Africa. It bites all warm blooded animals, including man, in the same manner as do other fleas, but in addition the pregnant female bores and ensconces herself in the subcutaneous tissues and there swells up to the size of a pea and matures her eggs. I was able to follow through the life history and to show that the accepted ideas concerning it were incorrect.

A specially interesting point brought out in these studies was that the "chiggers" have a predilection for the under side of the toes of man at the web of the foot and by causing a long-continued irritation give rise, by virtue of the inherent fibrogenetic tendency of the blacks, to the spontaneous amputations known as ainhum.

In this country there are many species of fleas, and a high significance is to be attached to their presence since Wherry has demonstrated that plague is endemic in the ground squirrels *(Otospermophilus beecheyi)* of the Pacific Coast. These animals together with their allies extend right across the continent as far as Nebraska, and it has been proven that the commonest fleas they harbor *(Hoplopsyllus anomalus* and *Ceratophyllus* acutus*)*, bite man also.* We have in consequence all the ingredients, namely, plague, rodents, fleas and man, essential for a possibly interesting situation, not only in the Pacific slope States, but also in the Middle West. One of our States, California, has thus taken rank with Southern Manchuria, Yunnan, China and Uganda, East Africa, and shares the distinction of being one of the four endemic plague centers of the world, from which at any time an epidemic may spring which might demand the graphic pen of another Defoe. I commend this picture to you as a subject for profitable meditation.

I might also point out before passing on that part of the life history of a common cestode (*Dipylidium caninum*) is stated to occur in fleas and that at least one Trypanosome *(T. lewisi)* has been experimentally transmitted from mammal to mammal through these insects.

Beetles.—I fancy I can detect an attitude of incredulity among you when I mention this order of insects as being of possible interest to us as pathologists. But the larvæ of our common *Blaps mortisaga* have often been reported as pseudo-parasites in man, and Daniels, a most careful observer, has mentioned a beetle larva occurring in an abscess of a man from Demarara.

Two beetles (*Acis spinosa* and *Scaurus striatus*) are said to be the intermediate hosts of tapeworms. Von Stein has found bladder worms in the larvæ of *Tenebrio molitor.* Braun states that

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* Since this was written, the wild wood rat of California *(Netonia anectens)* has also been found to be infected in nature by plague.

Blaps mucronata is the intermediary host of *Echinorhynchus moniliformis.* I myself found larvæ of beetles *(Drilus and Tetralobus)*, in Angola, which possess poisoned spines upon which the barefooted natives sometimes accidentally tread. When these spines enter the flesh they set up inflammation, at times so violent in type as to end in gangrene. The deadly arrow poison of the Bushmen is prepared from the grubs of a Chrysomelid beetle (*Diamphidia locusta*). Some of the large African Carabidæ (*e. g. Anthia calida)* eject with great force a strong smelling liquid from the posterior part of the abdomen, which gives rise to a severe irritative conjunctivitis should it reach the eye.

It should be remembered, too, that a coleopterous insect (*Platypsylla castoris)* is a natural parasite of mammals (beavers). It is dangerous therefore to exclude on *a priori* grounds this order of insects from the interest of the pathologist.

Lepidoptera.—A long list might be given of these insects which give rise to violent urticaria through the irritating substances contained in their spines and scales. In Africa I studied a large number, chiefly belonging to the Arctiidæ, Limacodidæ and Liparidæ. One very troublesome species is *Natada amicta.* A patient was even forced to return to Europe because of excessive susceptibility to this urticaria. There is a large literature on this subject, and the pathology of the condition has been well worked out. Many offenders from other parts of the tropics have been reported. In Europe the so-called processional caterpillar is familiar to all and here in America I personally know of one gentleman who was forced to resign from a scientific commission organized to study the brown tail moth in Massachusetts for no other reason than the suffering which contact with the insect produced in his case.

A moth (*Asopa farinalis*) has been stated to be a secondary host of at least one common cestode. I should mention, too, that one, if not two moths, are normally parasitic upon mammals. In South America we have *Cryptoses Cholœpi,* which lives on the great sloth. We cannot therefore exclude the possibility of it or other similar forms assuming importance to parasitologists.

Hymenoptera.—The stings of these insects are familiar to us all. In Angola large pugnacious bees (*e. g., Xylocapa rufa*) and large stinging ants *(Paltothyreus tarsatus* et al.) deserve mention.

Huge wasps of the genera *Scolia* and *Salius* are also feared. The poison of these is by no means a negligible thing[*].

Fatal cases of bee sting have occurred in this country and Europe, while wasp and hornet stings are often reported in medical literature.

The only case that has come to my attention of a Hymenopteron acting as a possible carrier of disease was reported some years ago from Cyprus by Williamson. He suggested that anthrax in that island was disseminated by a species of velvet ant (Mutillidæ), which was found under the carcasses of animals dead of the disease and which was often handled, especially by children. Both the insect and the disease are called by the natives sphalangi.

LECTURE II.

The Diseases of Portuguese West Africa.

In our last lecture we discussed the general subject of insect disseminators of human disease in the tropics, and to-day we take up a consideration of the diseases themselves which occur in a small portion of the tropical world. We can hope to do no more than deal with a single phase of it as it stands printed on the announcements, and perhaps a better title for this lecture would have been "Some of the More Interesting Medical Diseases of Portuguese West Africa."

Malaria. This is by far the most important infection seen in Angola. I can do no better than to give a brief resumé of a previous report on the subject. My observations were made at a point represented by Lat. 12° 13′ 30″ S. and Long. 16′ E., the altitude being 4,761 feet above the sea, and the mean temperature for a year registering 65.85° F.

The frequency of the disease is difficult to pronounce upon, yet by employing the spleen index, microscopical blood examinations and *post mortem* examinations of viscera I was able to reach some tentative conclusions, which I here give. In both blood examinations and spleen tests I employed good series (about 500 individuals in each group) and confined my statistics to cases which had never received treatment. This diagram shows that (after

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[*] For a few of the writer's observations on the medical entomology of West Africa, see *Deutsch. Ent. Zeitschr.*, 1907, pp. 17-20, 199-200,377-8, 584, etc.; *Bull. Soc. Ent. Fr.*, 1908, pp. 76-79; *Ent. News*, 1906, pp. 64-7, 294-302; 1908, pp. 26-33, 224-30; *Ann. and Mag. Nat. Hist.*, 1906, pp. 242-4; *Polytechnia* (Lisbon), 1906, pp. 2-7, 204-6; 1907, pp. 3-7, etc., etc.

FIGURE 1.
Blood Examinations of 531 Untreated Natives.

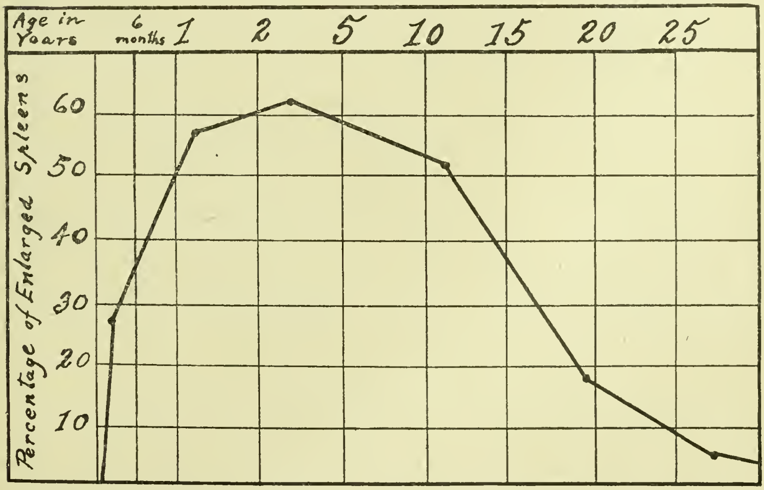
Total Number of Examinations	FORMS OF PARASITE				Large Mononuclear Leucocytes 20% or over	*Filaria Perstans*	Trypanosomes
	MALIGNANT TERTIAN						
	Small Intra Corp. Rings	Crescents	Rosettes in Blood	Quartan			
531	272	12	1	14	153	4	3

taking account of 18 instances of double infection which this form of statistics does not show) the percentages of blood infections were, in round numbers, as follows:

Infection with small malignant forms.........	51 %
" " crescents	2¼
" " quartan parasites	2½%
" " benign tertian	0 %
Count in which large monouclears exceed 20%..	29 %
Apparently normal individuals................	17%

A glance at Figure 2 shows the percentage of enlarged spleens. It is apparent that over 60% of the population become seriously

FIGURE 2.
Spleen Index of Untreated Natives (351 Children and 162 Adults).



infected after the third year. Taking this in connection with the fact that 83% of all examined are found to harbor parasites or other evidence of malaria in their blood, I conclude that moderate

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[*] *Atti della Società per gli Studi della Malaria,* Vol. VI, pp. 29-58.

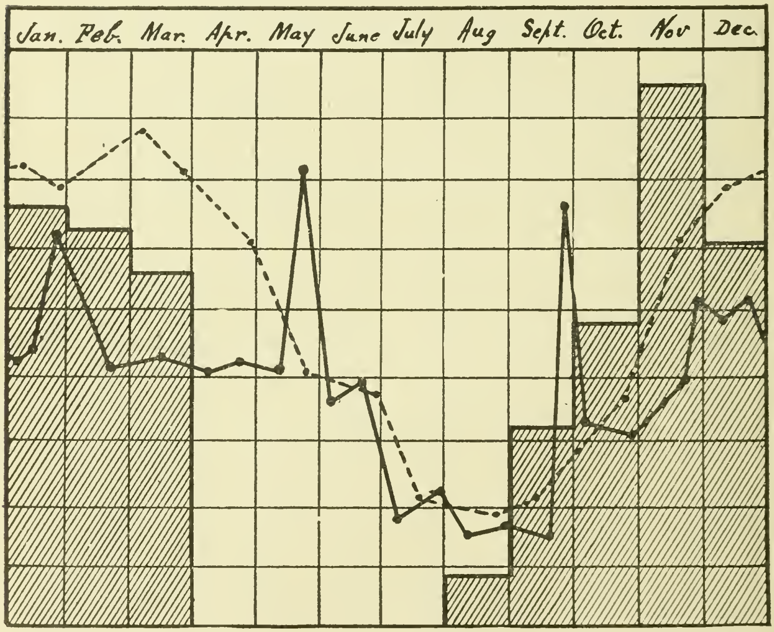
infection is almost universal and that at least half of the individuals are at times heavily infected.

The economic importance of the disease is considerable, as it necessarily interferes with service and lowers the value of the black as a workman.

I found the principal malaria-bearing mosquito of the region we are considering to be *Myzomyia funesta,* which I found infected in as high a proportion as 13% in one locality. I also demonstrated *Pyretophorus austeni* to be a carrier of the disease, about 1% of the specimens taken in one district showing parasites. I invite your attention for a moment to Figure 3, which brings out the interesting coincidence between rainfall, anopheline mosquitoes and malaria, and is from the records of a hospital once in my charge. The mosquitoes were always collected from a certain amount of wall space, and only the number of cases actually proven to have malaria were counted in making up this chart.

FIGURE 3.

Showing the Relation Between the Amount of Rainfall, Number of Anopheline Mosquitoes Taken, and Percentage of Malarial Fevers Among the Natives of One Station in Bihé District, Angola, for One Year.



Shading Indicates Rainfall.
- - - - - - - - - Indicates Comparative Number of Anophelines Taken.
———————— Indicates Comparative Number of Fevers Among Natives.

NOTE.—The epidemics of fever in January, May and September are probably to be accounted for by sudden changes in the weather stirring up latent malaria in the natives.

It has already been said that the ordinary benign tertian, which is so common in temperate lands and in many tropical climates, e. g., in Manila, was never seen in West Africa. The behavior of so-called tropical malaria or infection with the malignant tertian type has been well and carefully studied in Africa and voluminously described. So I will not weary you with a discussion of it. But no one has closely worked out the results of quartan infection in the tropics. I may therefore be forgiven for bringing before you some charts which set forth some observations made on an untreated case of this form of fever.* From Figure 4 we see the pulse and temperature for the week during which the

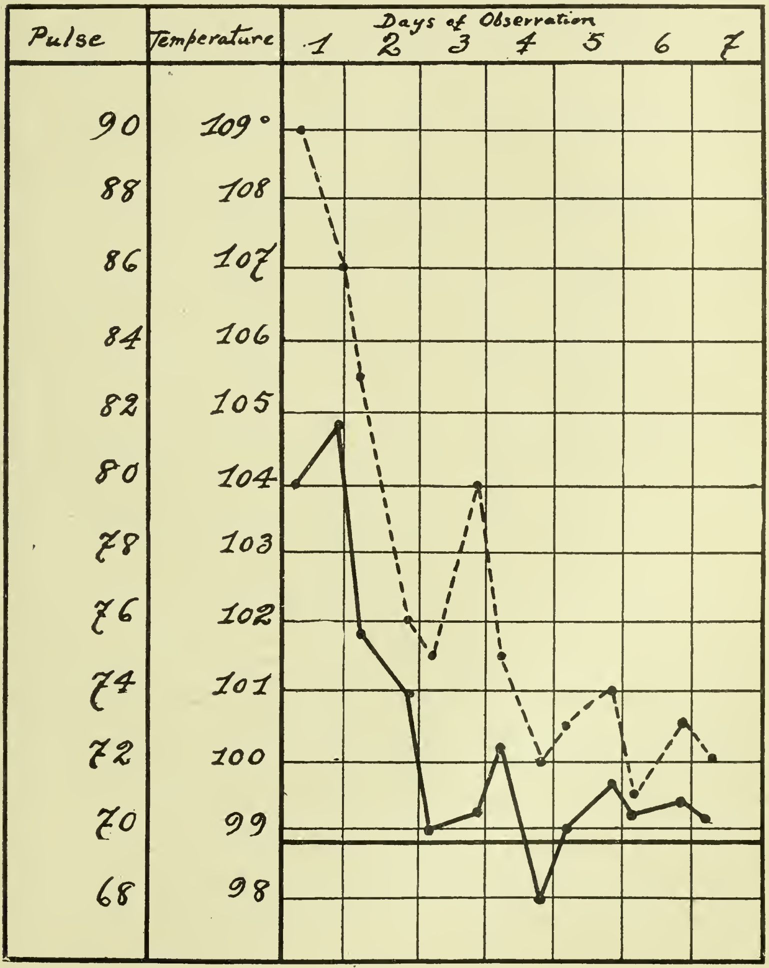


FIGURE 4.

Pulse and Temperature Chart of an Untreated Case of Quartan Fever in a Native.

EXPLANATION OF CHART.

———————— = Degrees of Temperature in Mouth (F).

- - - - - - - - - = Number of Pulse Beats per Minute.

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* Cf. Wellman. *Medical Record,* 1908, pp.1-7.

patient was under surveillance. In the next we see a graphic representation of the sporulation of the parasite in the patient's blood during the period.

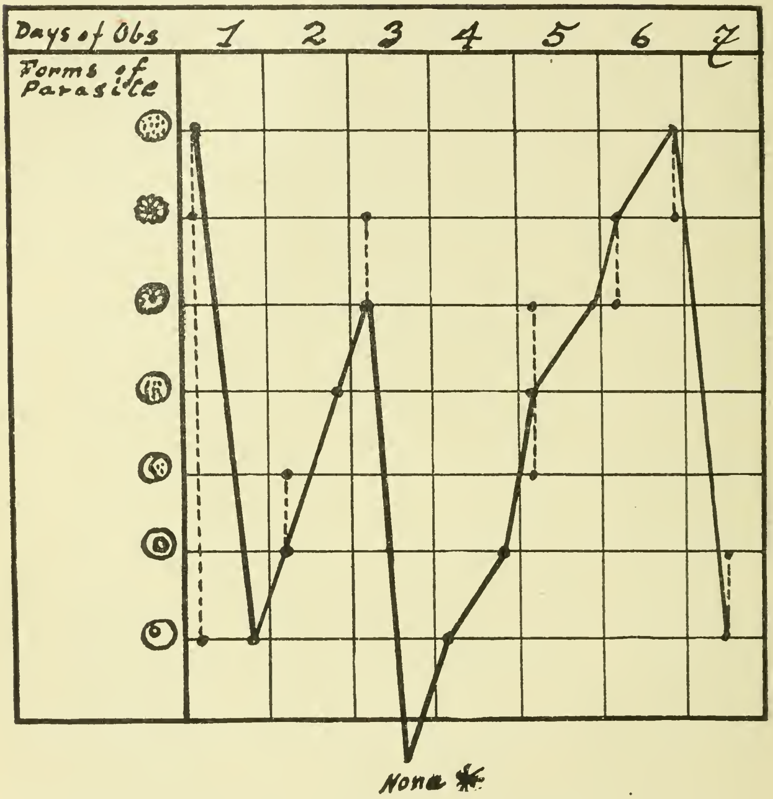

FIGURE 5.

Quartan Fever—The Stages of the Parasite Seen in the Blood at Different Times.

EXPLANATION.—The line representing the parasites refers to the developmental stages observed, and not to their abundance in the blood. The forms of the parasite are shown at the left of the chart.

* A few parasites (stage unrecognizable) were found on the evening of the third day in a thick film preparation stained with Romanowsky.

Figure 6 shows the comparison of the red and white cells at different stages of the disease and also the amount of haemoglobin present.

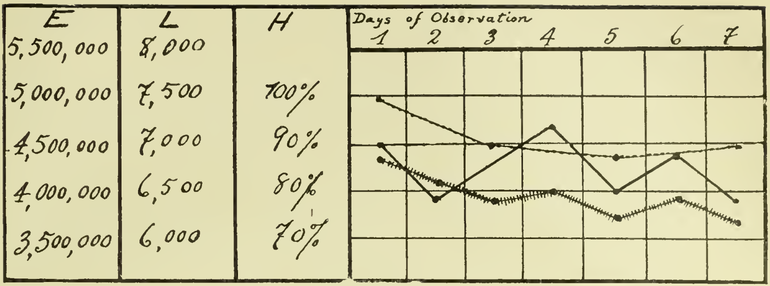

FIGURE 6.

Comparative Numbers of Erythrocytes and Leucocytes with Hæmoglobin Index.

EXPLANATION.

———————— = Erythrocytes (E).
- - - - - - - - - - - - = Leucocytes (L).
:|:|:|:|:|:|:|:|:|: = Hæmoglobin (H).

Figure 7 shows the comparative numbers of the different types of leucocytes.

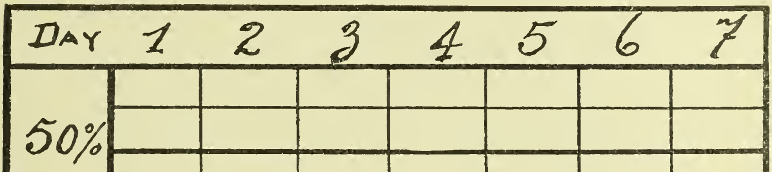

FIGURE 7.
Results of Differential Leucocyte Counts.

EXPLANATION.

.... = Percentage of lymphocytes.
———————— = Large mononuclears.
- - - - - - - - - = Polymorphonuclears.
—-—-—-— = Eosinophiles.

About 500 cells were counted each time. N. B.—The "Transitionals" were always counted with the polymorphonuclears.

Figure 8 shows the change in body weight and likewise the amount excreted by the patient during the period.

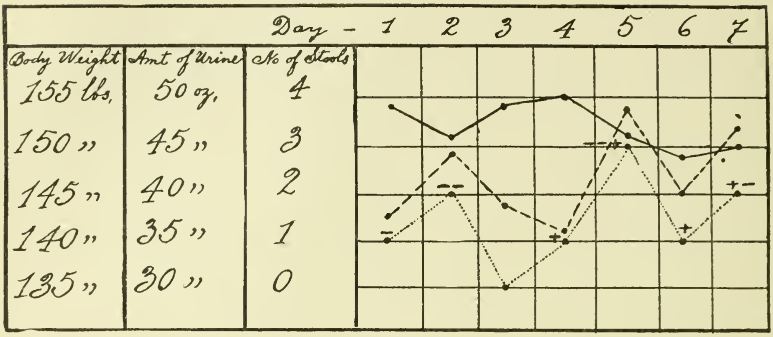

Figure 8.

The Change in Body Weight Compared with the Amount of Urine and the Number of Stools Passed During the Period.

Explanation.

———————— = Body weight in pounds.
— — — — — = Number of ounces of urine passed in 24 hours.
.... = Number of stools in 24 hours (+ = large stool, — = small stool.)

Figure 9 gives the food and drink taken by the patient.

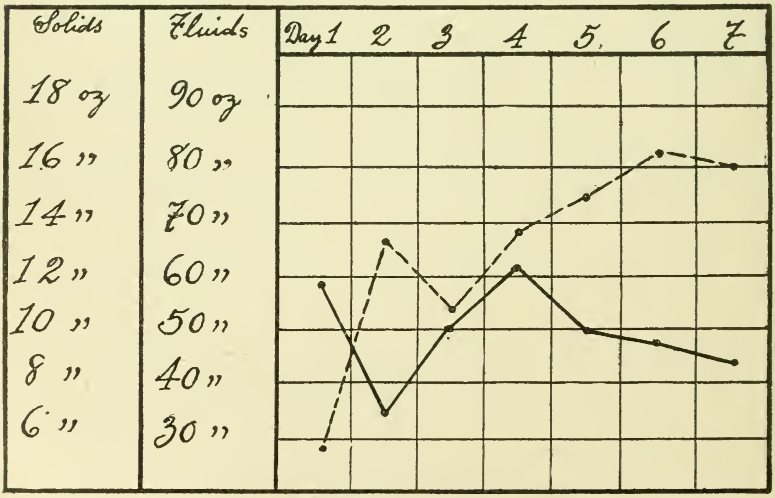

Figure 9.

Comparative Amounts of Fluids and Solids Ingested During each 24 Hours of the Observation.

Explanation.

———————— = Fluids in ounces.
— — — — — — = Solids in ounces.

From these charts it appears that quartan fever, which in America gives rise to quite severe symptoms, is a comparatively negligible factor in West African negroes, who have acquired sufficient immunity to live with comfort in districts swarming with malignant malaria.

Malarial infection is followed by many complications and evil consequences. One of these is abscess of the spleen.

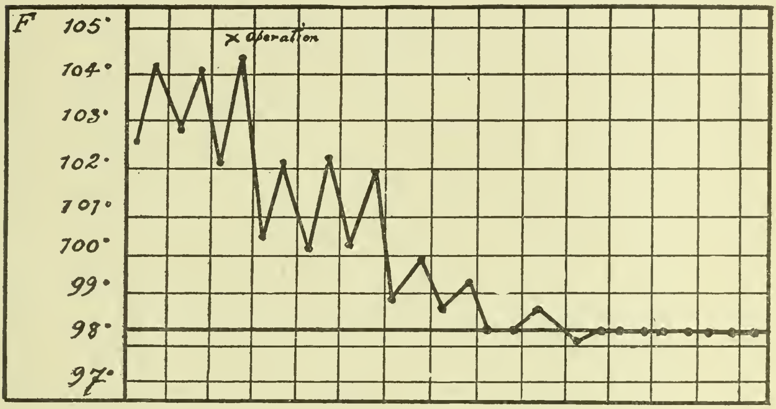

Figure 10.

Temperature Chart of Case of Malarial Abscess of the Spleen, Operation, Recovery.

Figure 10 shows the temperature chart of one case.

Blackwater Fever. This is the gravest disease of Europeans in Africa. Without pronouncing upon the question of the supposed relation of the disease to malaria, I may say that the principal carrier of malaria in West Africa, *Mysomyia funesta,* severe malarial fever and blackwater fever closely coincide in their distribution over the colony studied by me. Any depressing influence such as fatigue, exposure to cold, excesses of any kind, etc., may precipitate an attack of Blackwater fever or it may occur during the course of another disease. Figure 11 chart shows an instance of this.

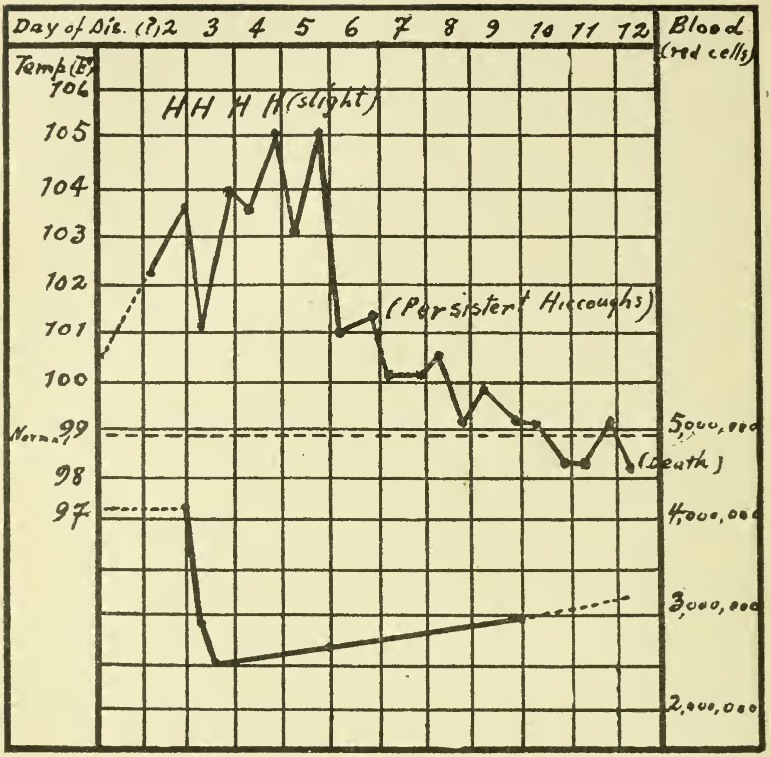

FIGURE 11.
Combined Blood and Temperature Chart of Fatal Case of Blackwater Fever Complicated with Amebic Dysentery, and Showing Malarial Parasites in the Blood.
H = Hemoglobinuria.

The sulphates are also said to predispose to hemoglobinuria, e. g., sulphate of quinin causing it, while the hydrochlorate does not. In West Africa the prognosis is of great importance. Roughly speaking, the danger increases in geometrical ratio with the number of attacks. My rule was to invalid home after each of the two first attacks and to refuse to pass a man to go out to the coast after the second. The treatment is symptomatic and unsatisfactory. I found intravenous saline injections of value in moribund cases with anuria. I have elsewhere suggested treating the patients in the earliest stages of the disease with serum obtained from immune natives living in very severe endemic blackwater districts.

Trypanosomiasis. Trypanosome infection, both of man and other animals, is exceedingly common in some parts of Angola.

In a report on these parasites I have especially studied the following species: *Trypanosoma gambiense* in man (*Homo sapiens*), *T. lewisi* in rat *(Mus natalensis)*, *T. aivum* in dove *(Treron calve)*, *T. Mega* in toad *(Rana tuberculosa)*. We will speak to-day only of the human parasite. Some of these cases showed practically no symptoms even while the trypanospomes were abundant in their circulation. One case was watched for about two years and from an apparently healthy condition went through the entire gamut of trypanosome fever into typical sleeping sickness. On inoculation into dogs the parasites appeared in the circulation after about a week and small pear-shaped developmental forms were numerous in the blood. Goats seemed to be immune to this trypanosome. Samples of atoxyl were sent out from Europe, but circumstances forbade the thorough testing of this form of arsenic as a therapeutic agent.

Regarding the important matter of prophylaxis, general rules cannot be laid down, but each district must be studied and suggestions drawn from the local conditions. The following preventive measure recommended by me for one district are illustrative of what be aimed at in drafting such regulations:

(1) The native camps at Esupua (the principal station on the way from the port to the interior and within a fly belt) to be moved farther away from the river and kept there by police.

(2) Squads of soldiers, etc., to be passed through the fly belts at night.

(3) Native quarters in the city of Catumbella (constantly visited by native caravans from the interior and partly within a fly belt) to be moved as fast as possible from the river to the hills north of the town.

(4) The government not to permit sleeping sickness cases and suspected cases of trypanosome fever brought from the endemic districts north of the Coanza River (or other parts of Africa) to be landed at Benguella or Lobito (the ports of the district to be guarded).

(5) Care to be taken not to allow such recognizable cases as already exist in the district to be transported (either from the coast to the interior or *vice versa*) through the fly belts.*

Uncinariasis. This infection is a frequent cause of anemia and death. In one district investigated 13% of the population were affected. In addition to the Old World hookworm *(Uncinaria duodenalis)*, I found in my district the New World form (*Necator americanus*) as well. This last form seems to be almost cosmopolitan, as it was sent me from East Africa and Rhodesia and has been reported from South America, Australia, the Philippines and other parts of the Far East, as well as from the United States and Europe. I found other species of hookworm in various animals, but these are not of special interest here. I should say that in one human case (infected with *U. duodenalis*) I observed the larvæ free and escaping from the eggs in recently passed feces, which is, so far as I know, a novelty. The embryos were typical and not to be mistaken for *Strongyloides* or other worms. In West Africa ground itch is not uncommon in the districts where uncinariasis occurs. The native black is the most often affected, but suffers less from the disease than does the European. The symptoms of the disease are well known and I will not detail them. In tropical Africa they are nearly always aggravated by malaria.

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* Cf. Wellman, *Rev. de Méd. et d'Hyg. Trop.*, 1907,pp. 1-3.

Dysentery. As is well known, the group of symptoms regarded as characteristic of dysentery may arise from one of several causes. It may be due to bacterial, protozoal or helminthal infection. In West Africa we had three principal forms of dysentery, namely, epidemic dysentery, probably due to Shiga's bacillus, endemic dysentery of amœbic origin and sporadic malarial dysentery. The first-named variety is by far the most fatal to the natives and carries off large numbers of troops, porters, etc., from time to time. Amœbic dysentery is not uncommon in whites, although, strangely enough, liver abscess is rare. A considerable per cent of apparently healthy natives have amœbæ in their stools. Dysenteric symptoms from malarial poisoning clear up quickly under quinin. Other forms of the disease resulting from protozoal infection are said to occur in the tropics. I have often seen an infusorian (*Balantidium coli*) in the feces, as well as various flagellate protozoal organisms, especially in conjunction with amebæ, but in my own clinic was not able definitely to connect them with the diarrheal condition sometimes existing in the patient.

Leprosy. Leprosy is quite common in Angola, but is not specially feared by the natives. Some searching in the historical records of the colony brought to light statements indicating the comparatively recent introduction of the disease among the indigenes. If it be true that the anesthetic form, or "nerve leprosy," is typical of races which have long suffered from the disease, one can postulate an opposite view from the received one, because in Angola this form of leprosy is very much more common than the nodular variety. The pathology of the disease is intensely interesting, due partly to the fact that the germ invades practically all of the tissues of the body and has a special predilection for the parts less richly supplied with blood, such as the nerves. The histological architecture of the lesions mark them as belonging to the so-called infectious granulomata and in patients where the system is inclined to react strongly to the invasion I have been able, by feeding, fresh air, cleanliness, surgical treatment of foci of sepsis and large masses of bacilli, and especially by the use of cod liver oil in generous quantities, to effect marked amelioration in many cases.

Tick Fever. This disease, first mentioned by Livingstone, has been long known in Africa, but has only recently been scientifically studied by Ross, Milne, Dutton, Todd, Novy and others, including myself. I was probably the first to show that the temperature and presence of spirochætes in the blood conform in some instances to typical cases of relapsing fever at home. The following combined blood and temperature chart of one of my cases shows this

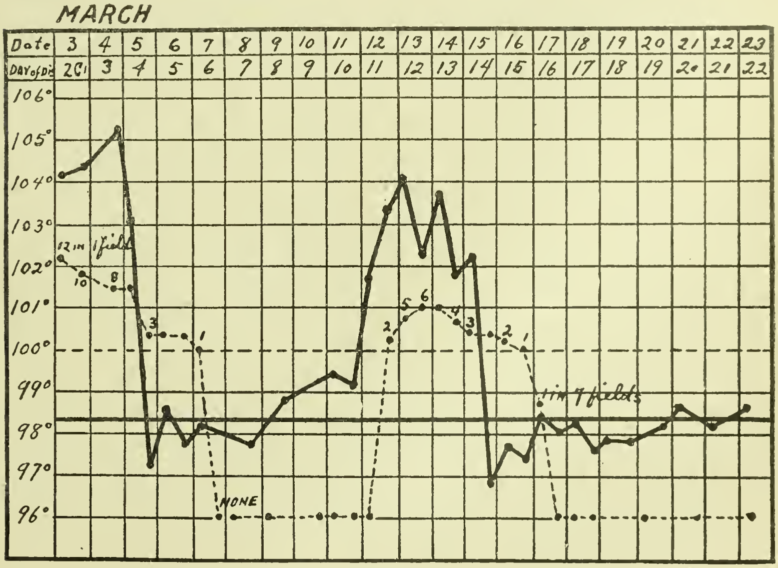

FIGURE 12.

Combined Blood and Temperature Chart of a Case of African Tick Fever.

DESCRIPTION OF CHART.—The Temperature is represented in the usual manner by an unbroken line. The dotted line represents the comparative abundance of the parasites in the blood during different stages of the attacks, taking the line marked 100° as representing the average of one parasite in each field. Thus, 101° would mean six parasites in each field, 102° eleven parasites, etc., etc.

well. The elucidation of the etiology of this disease is sadly linked with the name of Dutton, who lost his life from it while studying on the Congo. I was able by changing soldiers, etc., from beds to hammocks, the suspending ropes of which were wrapped in cotton, to protect them from the tick (*Ornithodoros Moubata*) which carries the disease and thus to stamp out a little epidemic in one district. In my capacity as medical officer I made several recommendations looking toward prophylaxis. The most important of these were:

(1) The tick in question should be regularly destroyed in crowded centers by disinfecting native houses, barracks and other permanent quarters and by burning old camps, huts, etc.

(2) Soldiers, laborers on plantations, etc., should be made to keep their houses clean and to sleep in hammocks or beds well raised from the floor and away from the wall. Natives should never be allowed to sleep in or near the quarters of the Europeans.

(3) Soldiers, porters, servants, plantation laborers and other controlable bodies of natives should be compelled to observe regulations regarding regular bathing and washing of clothes.*

Filariasis. The species of human filariæ found by me in Angola are as follows: *Filaria loa* Cobb., *F. bancrofti* Cobb., *F. perstans* Mans., *Filaria sp.*, and an undetermined embryo nematode in human blood (probably not a *Filaria*). The descriptions of the manner in which the adult *F. loa* wanders through the tissues, including the eyeball, has been known for a long time. The curious fact that the eye remains uninjured by this process is probably to be explained on the basis of the possibility of passage of one colloid body through another leaving no trace of its course, this possibility being due to certain ratios of surface tension between the two bodies.** It is thus we explain the passage of certain micro-organisms, e. g., spirochetes, from the anterior chamber of one eye to the anterior chamber of the other, or of bacteria through the walls of the alimentary tract.

The question of *Filaria bancrofti* and its relation to *Elephantiasis arabum* may be mentioned here. Manson's theory is the usually received one. On this hypothesis the adult female *Filaria* must be injured sufficiently to cause her to abort, but not to die;

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* *Vid.* Wellman, *Journal of Hygiene,* 1906, pp. 237-45.
** Cf. Fischer, *Jour. A. M. A.,* 1908, p. 833.

in other words, she must extrude eggs instead of developed embryos. These eggs are, unlike the young worms, larger than the lumen of the capillaries, and hence are unable to pass through the lymphatic glands, so a lymph stasis due to embolism of the lymphatic glands by these ova is predicated as the cause of tropical elephantiasis. This theory is ingenious, but is open to objections, one of which is that in West Africa I found districts in which infection by *F. bancrofti* was common, but where elephantiasis was rare, and other districts where elephantiasis abounded, but where the worm could be found but rarely or not at all among the population of the region.

Pathologically elephantiasis is a chronic edema associated with a connective tissue hyperplasia. The origin of this connective tissue overgrowth may well be sought in the chronic inflammatory condition which lies at the bottom of the elephantiasis. The causes for this inflammation may lie in the first instance in the chemical products of filarial infection aggravated subsequently by further infection by various bacteria. The theory which attributes the development of the edema to interference with lymph circulation is certainly inadequate, for ligature of all the lymphatics coming from a trunk limb is known to be incapable of producing an edema of that limb. I am more inclined to find the explanation of the origin of elephantiasis in the theory of edema advanced by Martin H. Fischer.* This author holds that the cause of edema rests primarily in the tissues. In consequence of various disturbances (circulatory, various poisons, etc.,), chemical or physico-chemical changes are produced in the tissues which confer upon their colloids an increased affinity for water and so swell. An increased absorption of water by the tissues therefore constitutes the edema. In applying these ideas to the question of elephantiasis we would have to say that through various agencies (of which filarial infection is one**) poisons are produced in the limbs or scrotum or other part of the body through which, by direct, or more probably indirect, means (acid production), the normal affinity of the tissue colloids for water is increased.

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* Martin H. Fischer, Physiology of Alimentation, New York, 1907, p. 268; *Jour. A. M. A.*, 1908, 51, p. 830; Kolloidchemische Beihefte, 1910, 1 Heft 3, where detailed reference to previous publications may be found.

** I have seen a man, who had never been out of England, with typical elephantiasis of the leg. v. Transactions of the Society of Tropical Medicine and Hygiene, p. 19.

The causes operating to produce the edema are lasting and associated with chronic inflammatory changes (deposition of connective tissue); as this is produced it, too, becomes involved, so that the final picture of elephantiasis is that well known to everyone, a chronic edema associated with an inflammatory connective tissue hyperplasia, itself edematous.

So it seems to me that the increase of lymph is not to be regarded as the cause, but as the effect of the edema; in other words, the attempt of nature toward resolution of the difficulty. And I am inclined to the belief that bacterial infection plays a great part in elephantiasis. Where ulcers abound in West Africa elephantiasis is also common. The strains of micrococci isolated from these ulcers showed high virulence and I have suggested that the same groups of organisms may be responsible for both affections, which are often seen together in the same patient.

Goitre. I investigated a notorious goitre district in West Africa and reached some conclusions regarding the disease. The goitre of warm climates is no doubt identical with that of temperate countries. We seem to get the same enlargement of the glands, with and without hyper, and hypothyroidism. I consider the usual parenchymatous goitre (together with the colloid form which is only a different type of the same process) as entirely distinct from the Graves-Basedow disease which may result in exopthalmos and other serious disturbances. Even in the most intense goitre areas the latter disease was absent. Cretinism also was extremely rare. The hypotheses advanced to account for goitre in the tropics are for the most part the same as those advanced for the disease in temperate climates. Among these are the following: That it is due to strong emotion or nervous excitement; that it is due to malaria; that it is caused by altitude and climbing; that it comes from living on calcareous soil, etc. I was able to exclude all these supposed causes and the half dozen other ones which have been advanced by the study of a single goitre infested district. In this district goitre was amazingly common while outside of it the disease was almost unknown. The region was peopled with men and women no more emotional than their neighbors, was freer from malaria than the districts surrounding it, had a lower altitude than several goitre free contiguous neighborhoods and was underlaid with a primary system of granite and sandstone, with absolutely no calcareous soil over the entire region. Several other less reasonable etiological hypotheses could be as definitely disregarded as those named. This observation bears out the well-known belief that parenchymatous goitre is a ''place disease'' like beri-beri.

Milk Pox. This scourge is closely allied to the small pox with which we are familiar in the United States and Europe. Thouands and thousands of natives are carried off by it every few years. Ordinary vaccine from London was efficacious against it, and we succeeded in creating among the aborigines a widespread demand for such prophylaxis. According to the native reports, an epidemic of milk pox is always immediately preceded by one of chicken pox. I saw this on two occasions myself. Other epidemics are known and dreaded. Two of these I identified as mumps and whooping cough, respectively.

Onyalai. This is probably a separate disease, although the cause is yet unknown. My original description was later followed by Massey, Mense, Feldmann and others. The disease is very fatal. Pathologically, its most striking features are purpura and peculiar hemorrhagic infarcts in the viscera. These infarcts are bacteriologically sterile. The disease possibly may be due to a protozoon.

Akatama. I first described this affection in 1903. Some of the cases suggest a modified Raynaud's disease. It is probably a mild peripheral neuritis. It may be malarial in origin although blood examination in a series of cases contraindicated this. The disease has been recently discussed by Balfour. Several other conditions first described by me may be mentioned in this connection. One is what I long considered an angiospastic neurosis signalized by pain in the upper chest. It is called "vonulo" by the blacks and "Bihê asthma" by the colonists. It has nothing to do with asthma or heart disease, and I now think it is probably due to osteo-arthritic exostoses (originating likely from the absorption of the products of digestive disturbances set up by intestinal parasites), which cramp the spinal nerves at their point of exit from the vertebræ.* Another widely known disease, by the blacks called "ochimumusu" and by the whites "land scurvy," has no relation to scurvy, but I demonstrated peculiar spirochetes different from the ordinary mouth spirochetes in the marginal ulceration of the gums which are the distinguishing mark of the affection.*

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* *Vid. Jour. Trop. Med.,* 1903, pp. 267-8; 1904, pp. 52-6; 1906, pp.1-4; *The Practitioner,* 1906, pp. 246-51.

Epilepsy. This affliction is very common, nearly every village having its epileptics. The disease is considered by the native blacks to be very contagious.

Yaws. This disease is a common complaint. I have already mentioned our discovery of the spirochete,* and that I consider it distinct from syphilis.

Helminthiasis. Uncinariasis and filariases have already been discussed. Other round worm infections are common. I have secured 90 ascarides from a child two years old, the result of a single dose of santonin and castor oil. Infection with these worms is almost universal in West Africa natives. *Trichocephalus trichiuris* and *Oxyuris vermicularis* are also common. Tape worms are not rare. *Dibothriocephalus latus, Taenia saginate, T. africana, Taenia sp. incert., Hymenolepis sp.* and several undetermined forms were seen. Flukes are also not rare. *Fasciola gigantea, F. angusta, Schistosomum haematobium, S. mansoni* and an unidentified species were found.

Myiasis. I sufficiently dealt with this question in my lecture on insects and disease. Several flies not before suspected of pathogenic significance were proven to attack man in West Africa.

Gonorrhea and *Syphilis.* These diseases were absent from Angola until imported by the members of a European Christian nation. Syphilis is known in the vernacular as "soldier's disease." I have mentioned in another lecture how both diseases are very atypical in the indigenes.

Craw-Craw. I have already said that this disease is really atypical scabies. Various other cutaneous diseases, e. g., ringworm, leucoderma, etc., are also common in West Africa.

Beri-Beri. A common and serious disease. In the island of St. Thomas and Principe I examined many cases during the epidemics there several years ago. Thirty thousand cases were said to be in the islands. I have seen numbers of white soldiers and officers in the colonial hospital at Lisbon who had been invalided home with the disease from West Africa. Both the "wet" and "dry" forms are seen. The most helpful treatment is prompt removal from the infected locality.

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* See Wellman, Arch. f. Schiff, Trop. Hyg., 1907, XI, p. 545, cf. Also, Woolley, *Internat. Clinics,* IV. p. 263.

Pneumonias. The disease in the sense we usually speak of it is, so far as I know, almost unknown; but a terminal pneumonia from various secondary bacterial invaders is not seldom seen. A true malarial pneumonia is not uncommon, and clears up like magic under quinin. I particularly mention these facts because in Angola cases with labored respiration from high temperature or other cause are often erroneously diagnosed as pneumonia.

Bites of Venomous Creatures. The bites of insects have been sufficiently discussed in a previous lecture. Snake bites were common in Angola. The most dreaded species is the puff adder *(Clotho arietans)*, which is found from Egypt to Cape Colony. In one case of bite from this snake I observed loss of coagulability of the blood after passing through the tissues at the seat of the wound, vomiting of blood, violent nose bleed (all, doubtless, from the direct action of the venom), and a remote action of the poison resulting in a peculiar jerky respiration. There was also sloughing of the site of puncture and the stirring up of a latent malarial infection.* Other poisonous snakes are the horned viper (*Bitis cerastes*), the house cobra (*Naja nigricollis*), etc. Many perfectly harmless snakes and lizards are considered by the blacks to be deadly.

Poisoning. The toxic agents employed by the natives of West Africa present a fascinating field for research. Many of these drugs are both obscure and potent, and a veritable reign of terror obtains in some regions from the machinations of the witch doctors and medicine men. I spent much time and effort while in Angola collecting and identifying the substances used as love philtres, therapeutic agents, arrow venom, ingredients in the poison test, etc., and give you to-day but a bare hint of the store of facts I accumulated.* I mention the plants under their native names. "Utata" (*Securidaca longipedunculata-Polygalaceæ*) is used by the native women to commit suicide. I gave four grams of what was said to be this plant in 30cc. of water to a large monkey (*Cynocephalus porcarius*) and produced death in 48 minutes, "Okalembe" *(Tephrosia vogeli-Leguminosæ)* is the widely used fish poison. "Okapilingau" (*Burkea africana-Leguminosæ*) is a favorite aphrodisiac. "Ombambu" (*Erythrophloeum guinense-Leguminosæ*) is the principal ingredient of the poison test by which thousands of natives perish in Africa every year. The bark of the aforementioned tree in small doses produces vomiting and purging; if powdered and inhaled it causes sneezing; the aqueous extract when injected under the skin of animals sets up vomiting, irritates and afterwards paralyzes the vagus nerve, causing the heart to slow and finally to stop. I administered a piece of the bark two inches square and one-half inch thick, ground up and mixed with soup, to a small dog. Its limbs were paralyzed in 21 minutes and it died in about an hour. "Nakanganga" (*Plumbago zeylanica-Plumbaginaceæ*) is administered to make an enemy sick and is thoroughly efficacious in this respect. "Ochimbinga" (*Strophanthus lanosus-Apocynaceæ*) is the plant, the milky juice of which is used, with *Euphorbia arborescens* (Euphorbiaceæ), *Hæmanthus toxicaria* (Amaryllidaceæ) and various animal substances, i. e., grubs of beetles (*Chrysomelidæ*), snake venoms, etc.—as arrow poisons. "Epangue" *(Cannabis sativa-Urticaceæ*) is "hashish, and is used—as is tobacco and cola (*Sterculia acuminata*)—for its pleasant effects.

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* Cf. *Am. Med.*, 1906, pp.94-9; *Medicine*, 1906, pp. 1-11.
* *Vid. N. Y. Med. Jour.*, 1906, pp. 1-4.

Other common disease conditions encountered in Angola are gundu, ainhum, keloids, "climatic" buboes (which I traced by means of cultures to coccic infection of small wounds in the lower limbs), multiple nodules, umbilical hernia and ulcers. Some diseases, such as enteric and liver abscess, are rarer than one would expect from the general health conditions of the colony. I failed to find a number of diseases, among which are typhus, scarlet fever, cholera, yellow fever, plague, Malta fever, pellagra, scurvy, anthrax, glanders (in man), *Arthritis deformans,* and gout.

LECTURE III.

Why the Physician in Temperate Climates Should Study Tropical Diseases.

I should be glad if the present lecture could be deemed in a large measure a work of supererogation, as the intimate trade relations now existing between the United States and tropical and semitropical countries and the still more intimate relationships that will grow out of the opening of the Panama Canal, ought to render unnecessary any special arguments concerning the necessity of the study of tropical diseases in America. Not only is it important that many physicians should have opportunities to become trained in tropical diseases, in order that they may meet the health problems confronting the native and the white man in the tropics, but tropical diseases are fast becoming a serious menace to the white man in his own country. Several of these already exist endemically in America, and others are constantly being imported, and, unless properly handled by trained men, they threaten danger not only to the communities in which they now exist but to the United States in general. But I am afraid that the warnings and exhortations which I plan to give at this hour cannot justly be deemed unnecessary. In other countries the activity along this line is gratifying. The establishment of schools of tropical medicine in London, Liverpool, Paris, Hamburg, Lisbon and other centers, the founding of journals of tropical medicine in England, France, Germany, Portugal and elsewhere, the inauguration of European institutes of tropical research in Africa, India, China, Japan and other parts of the Far East and other like projects, together with the enormous literature dealing with this department of medicine, all emphasize this activity. In America, while something is being done (both at home and in our colonies), which is excellent so far as it goes, we have not much to be proud of so far as general education of the profession and public in tropical medicine is concerned. In the hope of interesting you in this very important matter, I submit to you a few of the many reasons why the physician in the temperate climates should study tropical diseases.

1. *Because there are no tropical diseases.* I do not mean this statement as a pert paradox, but wish merely to emphasize the

fact that tropical medicine is an integral part of general medicine. This term "tropical medicine" has been justly objected to, and, while a convenient designation, is apt to be misleading to those whose interest in and knowledge of the subject is slight. Scientific medical men of course know that there are almost no tropical diseases in the strict interpretation of that term. In short, it is just as allowable to speak of tropical zoology or tropical botany as of tropical pathology—really, one might almost as well say tropical chemistry. All pathology is one, be it "temperate" or "tropical." Still the term has done good. It has been a watchword, it has stood for a fine type of specialization, and it has served as the expression of a point of view from which various important diseases new and old have taken on a different meaning, the practical outgrowth of which has in not a few instances meant the physical betterment of millions of human creatures. As a fortunate result of this, the time is fast coming when no one can claim to be *au courant* with the science of general medicine without an appreciative acquaintance with the leading facts of "tropical" pathology. To return to our paradox, we must not forget that many of the tropical diseases were once cosmopolitan and might become so again. Take, for instance, leprosy, which is commonly spoken of as a tropical disease. Three important endemic centers of this disease are still Iceland, Norway and Canada, none of which could be called tropical, to say the least. In Sir Patrick Manson's classical work on Tropical Diseases I find such affections as malaria, relapsing fever, dengue, etc., discussed, and rightly, notwithstanding that these diseases are common both to tropical and temperate countries. In the same book we may read descriptions of less known diseases, namely, yellow fever, pellagra, Rocky Mountain spotted fever, dysentery and uncinariasis, which either have been or are now endemic in our own country. The ancient devastations of civilized countries by plague and yellow fever may possibly be at an end, but the fact remains that we are at present impotent to drive at least two tropical diseases from our land, namely, pellagra, which is heralded as a "menace" in the glaring headlines of our daily papers, and hookworm disease, of which our best authority, Stiles, states that it is in some parts of the South reducing the laboring capacity of the people 60 to 70 per cent, and is therefore one of the most important factors in the inferior mental, physical and financial condition of the poor white population of that region. In matters of national health "eternal vigilance" is truly "the price of liberty." If we are to keep out of our land yellow fever, relapsing fever, plague, cholera, dengue and a dozen other diseases "once triumphant throughout Christendom, but which have been practically ousted from Europe and the temperate parts of America by the spread of civilization and the improved hygiene that has followed in its train" (Manson), we must bestir ourselves to study and meet these scourges. They have by no means died out, but persist in our tropical and sub-tropical possessions, from whence they constantly seek another foothold in the land of their defeat. The advantages for spread that modern transportation devices give these diseases cannot be overestimated.

2. The medical man in temperate climates should study tropical diseases *because the educated physician can afford to neglect no part of the science he follows.* Many illustrations of this statement might be adduced. Professor Scheube a few years ago wrote to all the best known workers in the tropics for data regarding venereal diseases in hot climates. Syphilis is probably the most interesting disease in the world, both clinically and pathologically, and the new facts and side lights on the disease brought out by this enquiry, which Scheube digested and published as a monograph, were highly important. I know of almost nothing of greater value to the syphilographer than a perusal of this brochure, which has been practically forgotten except by tropical enthusiasts. Even more valuable to the syphilographer would be independent study of tropical influences on the disease. Why, for instance, is it milder and more typical in the negro in West Africa while the opposite is true of the affection in the negro in South America? Many other equally engrossing problems await the interest and endeavor of workers who patiently turn over barren ground and rehash well-known facts about the disease as it occurs in their own State or country. Again, we take the closely allied disease known as frambesia or yaws. The clinical manifestations and histological architecture of this disease ally it closely with syphilis, which view is enormously strengthened by the finding in the lesions, independently by Castellani and myself, of a spirochæte morphologically almost indistinguishable from *Treponema pallidum.** Yet yaws is not a

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* *Vid.* Wellman, Arch. f. Schiffs-u, Tropen. Hyg.. 1907, pp. 545-7.

venereal disease, and no one who has studied the two processes side by side can escape the conviction that they are distinct, though analogous, entities. How much use is made by the syphilographer of so rare and fortunate a circumstance for the purpose of widening his horizon and grasping more intelligently the facts and relations which compose his field of research?

Let us now turn to a disease which, next to syphilis, is perhaps of as great intrinsic interest as any we know, besides having a special appropriateness as a subject of study because of its analogy to the plague of our race, tuberculosis. I refer to leprosy. In leprosy we have a disease the specific bacillus of which has been found in all the tissues of the body except the muscles. Imagine, then, the engrossing interest presented to the pathologist by the processes thus set up! And I believe that the treatment of the disease offers far more hope to the therapist than is generally conceded. While cases are constantly being imported, and imported foci of the disease exist in North America, yet the study of the whole question is relegated to specialists and tropical experts, or, what is far more illogical, to dermatologists. This is only one instance of such neglect. The shibboleth of American endeavor is in too great a degree immediate practical utility. One cannot be a physicist, he must be a teacher or an inventor. One cannot be an entomologist, he must be an "economic" entomologist. It is not to our credit that the American devotee of pure science must, if dependent on his work for a livelihood, usually expect to starve. This spirit, unfortunately, largely invades medicine. Let us not forget that the great "practical" discoveries that have blessed mankind have been in large part the incidents or by-products of purely scientific research, and in our profession, above all, let us not brand as "academic" or "impractical" the study and investigation of these too little known but highly important questions of tropical medicine, the lure of which may possibly lead some of my hearers to endeavor as great as that of a Manson or a Laveran.

3. Another reason why tropical diseases have a claim on our attention is that *a goodly part of recent medical research has been done in the tropics.* All are familiar with the brilliant work of Laveran, Manson, Ross, King, MacCallum and the Italians on the etiology of malaria. The same may be said of the demonstration by Finlay, Reed, Carroll, Lazear and their associates of the

means by which yellow fever is transmitted. I have heard this work referred to as one of the most brilliant and conclusive investigations in the history of pathology.

The observations of Castellani, Bruce, Dutton, Todd on sleeping sickness, with those of Leishman, Donovan, Rogers and half a dozen more on tropical splenomegaly might also be mentioned. The excellent work of Fritz Schaudinn on spirochætes, that of our own countrymen in the Philippines on amebic dysentery, the classical researches of Manson and Low and their followers on filariasis are all excellent illustrations of how the science of general medicine is being carried forward in the domain of "tropical" medicine. In fact, it is almost dangerous to single out for mention any small selection of names from the splendid army of those who have advanced and are advancing human knowledge in this great field. A glance at such works on tropical diseases as those of Corre, Roux, Davidson, Scheube, Manson, Mense, etc., make vivid to us a sense of the obligation we are under for the large additions to our general knowledge which they chronicle. Let us, then, as students learn more, and as instructors teach more of this new heritage of medical information.

4. A more distinctly practical reason why the physician in temperate climates should study tropical diseases is because *disease in the tropics throws light on vexed problems of disease at home.* I have already pointed out the close analogy between yaws and syphilis and how a study of the former throws light on the latter. The different behavior of the malarial parasites in hot climates from its actions here at home is an instance in point. It is a well-known fact that in hot climates the crescent-shaped gametocytes of the malignant form are very rare in the peripheral circulation. On the other hand, there is never any difficulty in demonstrating them in appropriate cases of malaria contracted in the tropics and afterwards invalided home.* The physical well-being of the patient in a healthy climate and the scarcity of appropriate mosquitoes, forces, so to speak, the parasite into a different sort of regime.

If you will forgive a personal reference, I wish to mention again that by studying in West Africa—a district heavily infected with goitre and entirely surrounded by goitre-free districts, I was able

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Cf. Wellman, *Deutsch. Med. Woch.*, 1906, p. 2

to exclude all the etiological theories yet advanced to account for the disease, including the drinking water hypothesis. I might also point out in this connection how the study of the tick fever of Africa has added materially to our knowledge of the relapsing fevers. In fact, many instances might be brought forward were it necessary further to point our moral.

5. The most immediately interesting and practical reason why the physician in temperate climates should study tropical diseases is because *these diseases are constantly being introduced into his own country.*

In the United States we are continually threatened from Mexico, the West Indies, South America and the Orient. Plague has secured what threatens to become a permanent foothold among the small rodents of California, and human outbreaks may, in spite of our best efforts to hold the disease in check, be expected in that State at any time.* The public knows of the outburst of cholera this last year in Russia, and no one can say how far one of these diseases introduced from the tropics may travel if once firmly introduced on our soil.** Leprosy is already a naturalized disease in the United States, and several cases, one of domestic origin, are at the present time under my observation. John D. Long, of the U. S. Marine Hospital Service, has collected in San Francisco a long series of cases of amebic dysentery occurring in individuals who have never been out of California. Uncinariasis, a disease imported from Mexico, or possibly with slaves from Africa, is one of the great problems of the day, as pellagra (another tropical disease) already exists among us as a scourge;*** yet these known diseases which threaten us may be as nothing compared to the unknown ones which wait an opportunity to attack us. Just as measles in Fiji, malaria in Mauritius and trypanosomiasis in St. Thomas Island, finding new and susceptible soil, nearly decimated the inhabitants, so some still unknown tropical disease now slumbering in a corner of one of our island possessions could be imported to bewilder our sanitarians, upset our cherished commerce and decimate our ranks. I do not say this is a probability, but it is a possiblity, and as such demands consideration from students of disease and from the public at large.

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* Since this lecture was delivered I have seen in California three cases of human plague within a few weeks, two cases coming from a rural district where infected ground squirrels are numerous, and the third case following closely upon the eating of some infected squirrels by the patient.

** Since this was written, cholera has been reported in Germany.

***I have recently seen a case of this disease in Oakland, California.

I hope I have convinced you that we need education in tropical medicine. I have several times been asked to place myself on record with definite suggestions as to how to carry on such a propaganada and I intend to do so to-day. I propose the following:

a. The establishing of *a course* (with laboratory facilities) *in tropical medicine in every medical school* in the United States. This course need not be very elaborate or detailed, but should include what every properly trained physician should know of the subject.

b. One or more *schools of tropical medicine* adequately endowed should be founded. Such may or may not be affiliated with a university or universities. In these the student who intends to live in the tropics or is specially interested in tropical disease should be able to find instruction in all that is known regarding tropical medicine. The staff of such a school should consist of a pathologist, a protozoologist, a helminthologist, an arthropodologist, a bacteriologist, a clinician and a surgeon. One of these should have general charge of the laboratories. In addition to laboratory and hospital work, lectures, demonstrations, recitations and written and oral tests should be held, the geography and epidemiology of disease receiving considerable attention. Scholarships by which promising students could secure a "wanderjahr" among the tropical schools in Liverpool, London, Hamburg, Paris, etc., would be needed, and prizes for research of a high order should be offered.

c. Selected students should be given opportunity to enjoy the facilities of *American research laboratories* already established in our tropical possessions and provisions secured by which these students would be admitted to similar institutions belonging to other countries. I have been assured that such an arrangement would be welcomed abroad.

d. *Research expeditions* to the tropics for the clearing up of specially interesting or immediately important problems should be sent out from time to time under the direction of the school.

e. A *journal* devoted exclusively to the publication of matter connected with tropical medicine should be founded in connection with the school.

f. Popular addresses and matter for newspaper publication should be provided when advisable by the school for the education of the public.

g. A *tropical section* should be opened by the American Medical Association at its meetings, where appropriate subjects may receive adequate discussion and through which any needful and legitimate influences on beneficial national legislation may be exerted.

A man of wealth could build himself no better monument than to establish and endow some such plans as these I have outlined, and to such a man his country would in turn be lastingly indebted.

LECTURE IV.

The Health Problems for Caucasians in Tropical Colonization.

The subject for to-day is not of my own choosing, but one upon which I have been asked by the University to present my views this afternoon. Were I speaking to an audience composed entirely of medical men I should doubtless emphasize the scientific problems in the tropics which are crying so loudly for solution. I might allude to the very incomplete state of our knowledge of the geographical distribution of disease, the inexplicable absence of some diseases from the tropics, the peculiar form which some cosmopolitan diseases assume in warm countries, the tropical ailments, the etiology of which is yet shrouded in uncertainty, the intermediate hosts which subserve various parasites and some of the myriad other questions which call our attention to the fact that the scope of tropical medicine is practically unlimited and its development still in its infancy. But I deal with a mixed audience in addition to the medical contingent for whom I originally came to this University. It seems best, therefore, to try to present a more general discussion than any yet attempted—a discussion of principles, in other words, and what technical details we find it necessary to introduce will, I am sure, be regarded as illustrative only.

Climate per se is not, as a rule, the problem to be faced in the tropics. With the exception of a few minor conditions, high temperature is not in itself the direct cause of any tropical disease. The causes of death and ill health in warm regions are rather to be sought in the endemic diseases which flourish in such countries and which may be only indirectly the outgrowth of a tropical climate.

I. Let us consider first *the problems which are presented by the diseases already endemic in tropical countries.* Many of the diseases rife in the tropics are caused by animal parasites. Now an animal parasite, be it a protozoan, a worm or what not, is usually dependent for its propagation upon two hosts, in one of which it develops and in the other of which it reproduces its kind. It is when one of these hosts happens to be a human being that the parasite becomes interesting to us as students of the diseases of man. The protozoan cause of malaria for example, develops in man and reproduces itself in the mosquito, that of filarial disease (small worms in the blood), develops in the mosquito and reproduces itself in man. It is obvious that if man is to protect himself from such enemies, he must be able to avoid or destroy the host which in common with himself is necessary to the existence and dissemination of the disease producing parasite. Many of these parasites are carried by insects, using the term in its widest sense. Such are, for example, malaria, sleeping sickness, relapsing fever, yellow fever, dengue and filarial disease. The continued existence of all these depends on animal parasites and all have been shown to be conferred upon man through the bite of insects. A striking example of how important a part insects play in the matter of health in the tropics is afforded by the American occupation of Cuba and the Panama Canal zone. By systematic destruction of mosquitoes and their breeding places yellow fever has been eradicated from these places, once hot beds of the disease, and malaria vastly decreased. It has been said that a large part of the French failure at Panama was due to a lack of proper sanitary measures, just as a generous portion of the credit for American success is due Col. Gorgas and his staff for their energy and enthusiasm in protecting the health and lives of those employed in the actual canal work. At Ismaila, on the Suez, Ross and his assistants practically eradicated malarial fever through scientific mosquito destruction. The work of Malcolm Watson at Klang in the Federated Malay States was hardly less successful in lowering the malarial fever curve in his city. Once in West Africa we prevented the introduction of sleeping sickness into a district simply by changing a caravan road which ran through a hot bed of tse-tse flies, and we stamped out a small epidemic of relapsing fever (carried from man to man by the bite of a tick), by replacing cots, up the legs of which the ticks could crawl, with hammocks in which the ticks could not reach the sleepers. Those who proceed to the tropics or deal with them should understand above all the *principles* involved in the prevention of the diseases endemic there.

It is often as important to avoid contact with the native races as it is to avoid the insect disseminator of disease. In the case of a malaria, yellow fever, hook worm disease and other affections the dark-skinned native is a sort of *tertium quid* in the situation. He harbors without much inconvenience to himself a parasite which, if conveyed to a white man, causes serious disease and death. The natives of West Africa go about in comparative health, even though their blood may be teeming with malarial parasites. If a proper species of mosquito bites such a native and then a white man the illness or death of the latter may follow. Thus we see how in laying out towns and designing dwellings in the tropics the indigenous peoples, as well as indigenous insects, must be taken into account by the white settler. It would of course be ideal if we could make the tropics a healthy abode both for the native and the white, but this is at present impracticable except in small areas. The question of personal phophylaxis thus becomes a problem to every white man proceeding to a hot climate. Without going into details let us say that four special rules should be kept in mind by anyone who would reside with impunity in the tropics.

a. The central nervous system should be protected from the actinic rays of the sun by suitable means such as wearing, while out of doors, a red or orange lining in ones hat and a strip of the same sewed into the back of ones jacket or shirt to cover the spine. In a helmet lead foil answers the same purpose.

b. Contact should be avoided as far as possible with native people and native animals. This is necessary to escape tropical ringworms, various intestinal parasites and other serious infections.

c. Only recently cooked food and drink should be consumed. This is the only way to avoid dysentery and other grave intestinal diseases.

d. The visitor or resident should above everything be protected from the bites of insects. Enough has already been said regarding the reasons for this rule. A "bell" mosquito curtain which tucks in under ones mattress is aboslutely indispensable, and every known device to kill and drive away household insects should be employed.

I have said nothing especially about the problems to be met in making the tropics more habitable for the indigenous people among whom we go and to whom we owe help and advice in such matters. The principles already laid down, however, apply to the black, yellow or brown man as well as to the white and since in the end we must be the teachers of the natives let it be borne in mind that nothing is so potent as example.

II. The second group of problems which claim our attention consists of those *created by the introduction into the tropics of new diseases.* It is a fact well known to students of the geographical distribution of disease that various diseases have invaded and become endemic from time to time in new territory. A disease common to one part of a country, but unknown in other parts, may suddenly appear in an entirely fresh district. This phenomenon has also taken place and is constantly taking place in the tropics, due principally to improved methods of transportation introduced by the white man in the course of his opening these regions of civilization. Thus we find malaria following the railroads in India and creeping higher and higher up the slopes of the Himalayas from year to year. Sleeping sickness has recently followed the trade routes in Africa from the west coast clear across the continent at the sacrifice of thousands of human lives. A striking illustration of the moving of a disease from one tropical country to another is the introduction of malaria into Mauritius. This beautiful island was until recent times free from malaria, when either the proper mosquito or the proper strain of malaria germ was introduced by ships from India. The disease swept in a raging epidemic over the island leaving in its wake a frightful mortality. The Seychelles and many islands in the Pacific are yet free from malaria, but the danger of infecting these healthy spots, so to speak, is constant and imminent. A still more alarming possibility and one which, Manson has declared, should be made a subject for international consideration is the possibility that yellow fever may, on the opening up of the Panama Canal, be transferred to Asia, the South Seas and East Africa. While ships must round Cape Horn or the Cape of Good Hope to reach these countries from Brazil and the West Indies (the home of yellow fever), the danger is nil because the cold latitudes to be traversed destroy the germs of the disease or the mosquito which carries them. When the canal is opened the entire voyage from the Antilles and the east coast of South America will be within the torrid zone and thus this dire possibility looms large before us.

Just as diseases may migrate from one part of the temperate world to another (for instance we have syphilis probably introduced from the New World to the old and small pox from the Old World to the new), or from one part of the tropics to another, so the diseases of temperate countries may be transported to the tropics and there gain a foothold. There are many examples of this. Measles, whooping cough, tuberculosis, leprosy and other diseases have within recent times been introduced from northern countries into the Pacific Islands. In our own country measles is regarded as a more or less trivial incident of childhood, but when it is introduced into the Fiji Islands the mortality was terrible, in some districts half the population dying. The explanation of this, and of the great mortality from malaria in Mauritius and sleeping sickness in Central Africa, is that when a disease is introduced into a new country it finds an exceptionally favorable soil for its propagation. Among races where it has existed for ages the processes of natural selection have resulted in a sort of racial immunity which is entirely lacking in these new victims who thus succumb by wholesale to its onslaught. And it is not only the immediate excessive mortality which is to be taken into account when a new disease is introduced into a country. Ross from his researches in Greece believes that the decline of the commerce, culture and importance of that country coincides with and is largely due to the introduction of malaria from Asia. So a subsequent prolonged and sad racial deterioration may also result from the establishment in any region of an alien disease. Another thought which must not be passed by is that when a new disease is once started on its wanderings no one can prophesy when it will stop. In a former lecture I mentioned the chigoe (*Sarcopsylla penetrans*), which, originally from South America, has invaded and entirely traversed Africa, entered India and has even been reported from Cochin China, and is evidently on its way round the world. This parasite gives rise to pain, mutilation and sickness, and is a capital illustration of how diseases due to animal organisms spread in these days of steamships and railroads.

III. This last group of problems, which I shall only allude to, contains *the problems which arise from tropical diseases which may gain a foothold in temperate climates.* To take one recent instance, you have doubtless all read of the epidemic of cholera which swept through part of Russia this last year, reaching even to the arctic circle, and which is now invading Germany.

In times past we have had here in America a taste of what diseases brought from the tropics mean to a nation, and this class of diseases exists among us to-day in far greater abundance than is generally suspected and new seed is constantly being introduced.

Now, to come to the crux of the whole matter, namely, the solution of these problems which I have outlined before you, what shall we say? Let us accept as our first axiom the statement that the solution depends on a better knowledge of the subject. What we need in this country is more study of tropical medicine. From an economic standpoint alone the matter demands attention. Let us premise two or three statments which can hardly be disputed, as follows:

a. The successful settlement of the tropics is of very great importance to the world.

b. Such settlement depends in no small measure on the solution of various hygienic and epidemiological problems there obtaining.

c. In the absence of this knowlege an enormous extra expenditure of lives and money is certain to ensue.

d. The problems in question can best be studied and met by trained observers working at first hand, in other words by scientific medical men living in the tropics.

If these statements, which seem to me self evident, be accepted as true, there is no need for me to dwell on the necessity for adequately equipped pathologists, clinicians and sanitarians, specially trained in the lines along which their investigations will run, to take up the enormous task awaiting them. It is little less than a cardinal sin to send a poorly trained man to the tropics, for even the inestimable advantages of being on the ground in the midst of fresh material cannot confer the ability to observe accurately. Institutes of research like those, for example, in the Federated Malay States, Manilla, and at Khartoum are steps in the right direction and are worthy of all praise, but the earnest individual worker need not hastily despair of adding his quota to the advance of knowledge in this great field. Granted the capacity for work and achievement, neither complicated apparatus, skilled assistants, nor unreasonable effort are necessary for the study of some of the most pressing problems which are being forced to our notice in the tropics. And as a career nothing offers finer prospects to the properly trained investigator. Manson has well said that the tropical worker "enjoys opportunities for original research and discovery far superior in novelty and interest to those at the command of his fellow enquirer in the well worked field of European and American research."

Turning finally to the possibly more selfish side of the question namely our own self protection here at home, the need of the situation is the same—more education, in this case not only of special students fitted for research, but of the whole rank and file of the medical profession, especially undergraduates in our medical schools (our future physicians), not omitting the laity, for every one is more or less a physician and a sanitarian in his own house. The fact that an increasing number of cases of serious tropical disease are constantly occurring, often undiagnosed and hence improperly treated and guarded, in our midst is not alone the fault of our medical practitioners but also of our medical schools. I have already in this course advocated that laboratories and instructors devoted exclusively to the subject of tropical medicine be inaugurated in our schools and universities. In my recent tour, including such diverse points as

Washington, D. C., Omaha, New Orleans and San Francisco, I found no place where material for such instruction was wanting. I have in a previous lecture outlined somewhat in detail a plan for better education in the matter of tropical medicine and shall not repeat myself to-day, but would like to close with the suggestion that the medical school of this university be one of the pioneers in this great movement.

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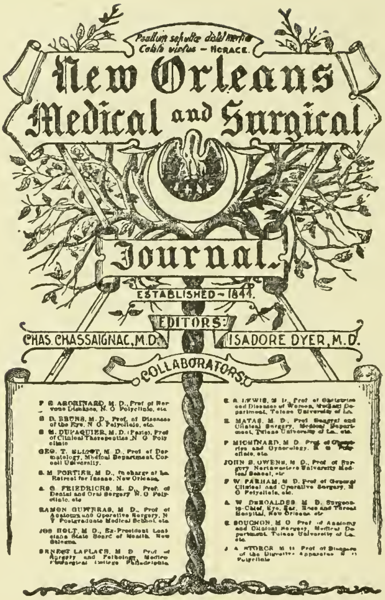
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VITAL STATISTICS OF TWELVE TOWNS IN THE ISLAND OF CEBU, PHILIPPINE ISLANDS.*

For the Seven Years From 1902 to 1908.

BY

ISAAC W. BREWER, M.D.

Manila, P. I.

A study of the births and deaths in any country is of interest not only to the medical student but also to the sociologist. Unfortunately the records of births are rarely accurate. It is believed that in the Philippine Provinces the records are fairly accurate. Nearly all of the natives are members of the Roman Catholic Churches, and, as a class they are very religious, and would not think of omitting the rite of baptism. The fees from this source are one of the principal means of support of the local church, and it is reasonable to believe for this reason if for no other the number recorded would be as large as possible. I have several times compared the records of births and deaths kept by the municipal authorities with those kept by the church and have found that they agree very closely. General J. P. Sanger accepted this view of the matter in compiling the statistics published in his report of the Census of the Philippine Islands.

This subject was brought to my attention through a paper by Musgrave and Richmond on Infant Mortality in Manila. That communication showed that the death rate greatly exceeded the birth rate, and that the mortality amongst children under one year of age was something like 71 per cent. of the births. As these figures did not agree with the impression obtained from residing in the Provinces, an endeavor was made to collect information upon the subject by sending out circulars to all the towns on the Island of Cebu. Answers were received from but twelve mucipalities which form the basis of this report.

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Cebu is a long, narrow island, traversed from south to north by a range of mountains of moderate elevation. The narrow coast belt of land is level and very fertile and most of the inhabitants dwell in the towns of this region. Their food consists of fish, corn, millet, rice, vegetables, fruits and an occasional meal of pork or beef. The quantity of rice consumed is much less than in many other provinces.

The climate is hot, but the rainfall is more evenly distributed than in other portions of the Island. The precipitation is greatest from July to November, and least during April and May but there is generally sufficient for agricultural purposes throughout the year.

The Island of Cebu was the first portion of the Archipelago to be subjugated by the Spaniards. Magellan landed at the present city of Cebu in 1521 and was killed on the Island of Mactan, which is just opposite the city.

The data here presented cover the years from 1902 to 1908 inclusive. During that period there were 40,382 births, and the deaths were 18,887 or 47 per cent. of the births. This percentage varied greatly, being as high as 67 per cent. in some localities and as low as 22 per cent. in others. This percentage compares very well with that obtained by General Sanger from the records of the Religious Orders. He recorded 199,898 births on the Island of Cebu during fourteen years between the years 1876 and 1907, the deaths being 49 per cent. of the births.

It is difficult to find tropical statistics to compare with those presented here, but from the report of the Madras Presidency we are able to obtain the births and deaths for the years from 1906 to 1909, which show the deaths to be 78 per cent. of the births. In the City of Calcutta, as in the City of Manila the recorded births are less than the number of deaths. The register of vital statistics for the Philippine Islands, informs me that not all of the births in the City of Manila are recorded, but that the records from Cebu are much more accurate.

On the Island of Cebu the deaths of children under one year average about 9.8 per cent. of the births. The largest rate was 15 per cent. and the smallest five per cent. According to Albert, in Manila, the deaths of children under one year of age are 47.6 per cent. of the births.

An endeavor was made to ascertain the cause of this great mortality, but no accurate data upon the nursing of children could be obtained. A general impression was formed, that most of the mothers nursed as long as possible, nearly always until the end of the first year, but that they also gave the child boiled rice and other foods at an early date. When a mother is unable to nurse her child she resorts to canned milks of various brands, generally the condensed milks. Sometimes rice gruel is used and the milk of the coconut and tuba, a drink made from the sap of the coconut tree are not infrequently made to take the place of milk.

The various departments of the Insular Government are endeavoring to improve the condition of the Fillipine people in every way possible but the field is so large and the workers so few that it will be a long time before much improvement in the death rate can be expected.

One of the greatest desiderata is physicians. In Manila and a few of the larger towns there are physicians, but in the smaller towns and the rural districts there are none. On the Island of Cebu, with a population of over 600,000, and a density of population of 337 per square mile, there are no physicians excepting in the town of Cebu. A large portion of the inhabitants of the Island are born, live and die without ever having the services of a physician. Here and there Americans have established small hospitals, but there is a great field for more. The expense will be slight compared with the great returns to be had. If some of the money which now goes to China and other Asiatic countries for hospitals could come here the returns would be as great if not greater. An enthusiastic physician, with a few nurses at his command, could, if located in a provincial town, do more to elevate these people than any other worker. It is hoped that some of the philanthropic people of our country will look into this matter and help us. Any of the churches that have been established in the Islands will gladly undertake the work, but it would be best to conduct it on a non-sectarian basis.

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A LIST OF THE TROPICAL DISEASES OBSERVED IN THE REGION OF SAN FRANCISCO BAY, CALIFORNIA.

By Creighton Wellman, M. D.,
Oakland, California.

(From the Laboratory of Tropical Medicine, Oakland College of Medicine.)

(Published under the Imprimatur of the American Society of Tropical Medicine.)

It is not realized by many that San Francisco Bay is one of the chief guardians of the health of the nation, that California occupies a special position of responsibility to her sister States in the matter of tropical disease. Not only are tropical diseases of many sorts being constantly introduced through the Golden Gate, but it should be remembered that much of California with its equable climate must be classed by the student of the geography of disease as part of the subtropics. There is no winter to break in upon the routine of tropical parasitic infections which may be imported and they are consequently able to become endemic. Malaria, rodent plague, and amœbic dysentery are all three illustrations of this remark. During several months of study and teaching the writer has encountered and had reported to him in the region of San Francisco Bay a number of tropical diseases of which a list is herewith given with brief notes on the various diseases. It will probably be a matter of surprise to some that so long a list of tropical affections are found in any locality in the United States.

Amœbiasis. The attention of the physicians of

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the State is being daily directed to what is a serious situation, namely, the presence of endemic intestinal amœbiasis in California, especially in San Francisco and Oakland. A number of medical men have taken up the subject somewhat specially so that cases are being reported at rather alarmingly frequent intervals. The writer has seen several cases quite recently, some of which originated in Oakland. One little outburst was instructive as being traceable to the water supply of the victims. The number of cases originating around San Francisco Bay is large enough to justify a conference to discuss the medical and civic aspects of the disease. Dr. John D. Long, of the Marine Hospital Service, has made some valuable observations of the disease as it occurs in California. He found that many of the cases arise in persons who have never been abroad, and suspects that Chinese vegetable gardeners are in many instances to be credited with carrying the disease. Through the kindness of Dr. Dudley Smith, of Oakland, I have had a case of amœbic dysentery under observation for months. This case is remarkable from the large number of atypical ulcers in the rectum. These have largely cleared up under initial enemata of quinine solution followed by the administration of ipecac, but the disease still persists after several months' treatment. I have also seen several cases of liver abscess supervening on amœbic dysentery, and one interesting case of amœbic appendicitis was brought to my attention by Dr. Long. A peculiar feature of amœbic disease is that, as in some other infections, the products of the prolonged intestinal indigestion are slowly absorbed and produce what may be designated as irritative osteoarthritic exostosis, chiefly on the spinous processes of the vertebræ, and these in turn give rise to stiffness of the back, pains, and even atrophy of different muscles from pressure on the spinal nerves at their point of exit.

Beriberi. Two cases, both in Chinamen from the region of Singapore, seen by me must be classified under this heading. A special investigation taking in all the ships arriving from the far East would doubtless result in the recognition of numerous cases. Both the cases seen were of the dry form of post-beriberic paralysis.

Bubonic plague. I have seen three cases of plague in man and also cases in rats and squirrels. Dr. Colby Rucker, of the Marine Hospital Service, gave me some weeks ago the following data: The wild ground squirrels are infected with plague to the extent of 1.6 per cent. in Contra Costa county. This estimate is based on a series of 20,000 animals. The number infected in Alameda county is over one per cent. Both these counties border on San Francisco Bay. Whenever a focus of infection is found the infected squirrels sometimes number over ninety per cent. of the whole. In one locality (West Hartley) fourteen out of twenty squirrels were infected. The infection has spread as far from San Francisco Bay as Hollister (about one hundred miles). At two places (Lafayette and Walnut) ninety-five per cent. of the squirrels sent in were infected, and the air was polluted with the stench of dying squirrels and the debris left by scavenger animals. The mouths of the deserted burrows were brown with fleas which greedily attacked man. These fleas were chiefly *Hoplopsyllus anomalus.* In Santa Clara county infected squirrels were found as far as fifteen miles below San Jose. San Benito, San Joaquin, Stanislaus, Monterey, Fresno, Merced, and Santa Cruz counties are all involved and the area of known infection now covers 4,000 square miles.

It will be seen from these facts that the residents of this territory are living on a slumbering volcano. Since Wherry demonstrated plague to be endemic in the wild mammals of the Pacific slope California has taken rank with Yunnan, Manchuria, and East Africa as one of the permanent endemic foci of the disease.

An interesting discovery by the Marine Hospital Service is that the wild wood rat (*Neotoma fuscipes*) is also infected in nature by *Bacillus pestis.* This rodent is an upper and lower Sonoran form and one of its allies is a boreal form extending into the high Sierra. As the infected species is found from Oregon to Lower California, etc., the deserts of Arizona, etc., the discovery is of great interest and importance. The fact that two genera of wild California rodents have been shown to harbor plague suggests the possibility of a general infection of the indigenous small rodents obtaining in the near future.

In Contra Costa county from 1903 to 1908 there were seven cases of rural plague of which six were surely traceable to squirrels, and all three of the cases seen by myself were also due to contact with these animals.[1]

Cochin China diarrhœa. Several cases of this disease have been seen. The free living generation of the strongyloides is easy to recognize in the fæces.

Endemic hæmoptysis. One case, occurring in a Chinaman from Formosa, was seen in which the ova of *Paragonimus Westermanni* were demonstrated in the sputum. A second case of what is almost undoubtedly this infection in a white man has been brought to my notice. The victim in the latter case had resided in Japan.

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[1] Since this was written a case of human plague has occurred at Hollister, in Monterey County.

Filariasis. Several cases of this infection may be reported here. Series of night blood have not yet been taken and it is probable that investigation will show the condition to be not rare. One very interesting case was brought to my notice by Dr. Edward von Adelung, of Oakland. The patient, a Japanese, showed microfilariæ in his night blood, and when first seen was suffering from a severe hæmatochyluria his urine resembling bloody milk. The case was kept under observation by Dr. von Adelung and myself and treated after the method of Wherry and McDill, i. e., exposure to the x rays over the mesentery after profound cinchonization. The hæmatochyluria cleared up like magic, the urine becoming perfectly normal, not even showing a trace of albumin. The embryos, while greatly reduced in numbers, still persist in the blood. The microfilariæ themselves were interesting in that they, while sheathed, showed the locomotile characters described for *M. philippinensis* together with the nocturnal periodicity of *M. Bancrofti.*

Gangosa. I have had the pleasure of seeing this terribly mutilating disease through the kindness of Dr. Simons and Dr. Geiger, of the Naval Hospital at Vallejo. Dr. Geiger has made some valuable and interesting observations regarding its ætiology and treatment. A full discussion of the subject will appear in a future communication by Dr. Geiger and myself.

Intestinal parasites. While not all the parasites about to be mentioned are tropical in origin, yet it has come to seem natural to list animal parasites with tropical diseases.

Ascaris lumbricoides. I have seen several cases. One case occurring in the practice of Dr. Edward von Adelung was an American who had resided in Japan and showed a heavy infection, passing adult worms on treatment.

Dibothriocephalus latus. One case seen, the patient being a Norwegian sailor.

Flagellate protozoa. One instance of heavy intestinal infection with *Lamblia intestinalis* has been found. This parasite is easy to distinguish because of its large peristoma. The only symptom was moderate diarrhœa. In a large percentage of the cases of amœbic dysentery a flagellate organism (probably *Trichomonas intestinalis*) may be seen together with the amœbæ. These monads also occur in the fæces of some healthy persons in California. Pigs in Alameda county frequently harbor a species of infusorian (*balantidium*).

Flukes. Trematode eggs were found in the fæces of a woman from Hawaii. The eggs of what is probably a *diocrocœlium* was once seen in the fæces of a dog in Oakland.

Hookworm. Several cases of this disease have been reported to me. One case was brought to my notice by Dr. E. N. Ewer, of Oakland. Through the kindness of Dr. W. A. Clark I have had the opportunity of keeping an instance of severe infection under careful observation recently at the Alameda County Infirmary. One of the endemic centres of the disease seems to be the Sandwich Islands, and former residents of that territory are constantly introducing the worm into California.[2]

Hymenolepis. One imperfect specimen has been received. I may say that *Dipylidium caninum* is very common among the dogs of Oakland.

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[2] Since this paragraph was written there has been reported to me a case of hookworm in a man who had never been out of California, besides several cases occurring in mines. The eggs and worms were found in these cases, which is of great significance.

Oxyuris vermicularis. Several cases have been seen in children.

Tænia solium. One specimen was sent in, without the head.

Tænia saginata. This worm seems to be common and a number of cases have been observed and specimens from other cases sent in.

Trichocephalus trichiuris. Very common, as a large proportion of those who have been in the Philippines for any length of time become infected. Eggs have been found in the fæces of patients from different parts of the far east. One woman direct from Italy and who had never been abroad before, showed ova in her stools.

Leprosy. During several months' study of a small group of lepers at the Alameda County Infirmary (Oakland) the writer has become much interested in the presence in California of this (to the pathologist) most fascinating of all diseases with the possible exception of syphilis. The invasion by the germ of all the tissues except the muscles coupled with the comparative immunity of the vital organs produces a remarkable disease picture. This was strikingly exemplified in an advanced case which recently came to autopsy by Dr. Martin H. Fischer. I have recently seen a leper on the streets of Oakland and Dr. Thomas J. Clark reports having noticed two or three more besides having had two in his private practice and one in his clinic at the Oakland College of Medicine. Dr. Fischer has called my attention to a case occurring within a few miles of San Francisco Bay in a white man who had never been abroad. Nodular, macular, and mixed leprosy have all been seen by me. The State could well consider the establishment of some special means of caring for the not inconsiderable and doubtless increasing number of leprous unfortunates within its borders.

Malaria. While there are many patients with malaria constantly entering California from the Orient, there are also numerous cases originating within the borders of the State. Dr. Eleanor S. Bancroft, of the University of California, has kindly furnished me with a record of the malarial cases treated in the students' dispensary infirmary during the past eighteen months, and these show that over two thirds of the cases originating in the State come from places on the Sacramento river or its tributaries. All the California cases I have seen came from the Sacramento or San Joaquin valley. Humboldt county in the north and Fresno county south have also furnished cases in Dr. Bancroft's experience, while one case seems to have originated in Oakland and another in Berkeley.

All three species of plasmodia have been seen. In my experience cases contracted in the Philippines are usually benign tertian while those from the Sacramento valley are chiefly æstivoautumnal with frequent double infections, the other parasite being benign tertian as a rule. It need hardly be said that no account has been taken of cases which were not recognized microscopically as well as clinically.

Pellagra. This popular disease is not wanting in California. Several instances of suspected pellagra have been shown me. One case, now at the Alameda County Infirmary, is extremely typical, the tongue, digestive symptoms (including regurgitation and the character of the stools), eruption, eye, and mental symptoms all being classical. It is interesting to record that this man, while emaciated, has a comparatively large number of red corpuscles and a good hæmoglobin index.

Schistosomiasis. Dr. Herbert Gunn has published records of a case of this infection in San Francisco. *Schistosomum japonicum* should be continually looked for as it may at any time be introduced.

Skin Diseases. But few observations have been made. Dr. Thomas J. Clark has reported to the writer an interesting case of Dhobie itch in which he demonstrated the causal fungus. The patient was from the Philippines. Dr. Clark also recently showed me a case of ringworm from southern Mexico. The patient stated that the native servants in that country are almost universally affected.

Sprue. Dr. Herbert Gunn has reported three cases to the writer and a fourth case has been referred to me since this article was begun.

The preceding list of affections (the result of a very short period of observation and enquiry) is significant as partially indicating the extent of invasion of our country around its great western port by tropical disease, and constitutes a strong argument for a widespread instruction in tropical medicine in our medical schools. Further investigation will doubtless add to the present list. It may also be pointed out that it is no longer necessary to go abroad for clinical and pathological material to study tropical medicine as few regions can furnish a longer list of tropical diseases than the Pacific slope of the United States. Finally, it may be said that an acquaintance with the methods of recognizing and combating tropical disease has become a practical desideratum even for the medical man who has no intention of practising abroad.

619 MARIPOSA AVENUE.

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A RESUME OF CASES OF MALARIA AND OF CASES SUSPECTED TO BE MALARIA, EXAMINED IN THE PAST THREE YEARS.*

(FROM THE POLYCLINIC LABORATORIES.)

By JOHN M. SWAN, M.D.,
Medical Director, The Glen Springs,
Watkins, N. Y.

After the inauguration of the course in Tropical Medicine at the Philadelphia Polyclinic, in January, 1907, the physicians in the Polyclinic Hospital were kind enough to refer to me for examination all cases of malaria and all cases in which malaria might be a factor in the clinical course of the disease from which the patient was suffering. I have selected some of these cases for the purpose of this paper, in order to illustrate some of the facts concerning the diagnosis of malaria and to illustrate some conditions that might be diagnosticated malaria clinically, when, as a matter of fact, that disease had nothing to do with the symptoms. The cases include nine of malaria, four of benign tertian infection, two of quartan infection, one of estivoautumnal infection, one of latent malaria, and one of pulmonary tuberculosis and benign tertian infection; one case of sepsis following an operation on the female pelvis; one case of tuberculosis peritonitis; one case of cerebral abscess; one case of splenomegaly; one case of myocarditis; one case of stricture of the urethra; one case of empyema of the gall bladder, and two in which a definite diagnosis was not made.

In the final lecture in his course on tropical diseases at the London School of Tropical

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*Read at the Seventh Meeting of the American Society of Tropical Medicine, St. Louis, Mo., 1910.

Medicine, Sir Patrick Manson is in the habit of advising the students in examining a patient from the tropics to bear in mind that the patient must not necessarily have a tropical disease; never to accept the patient's diagnosis of his condition, and never to accept another physician's diagnosis of the condition. He emphasizes the necessity of endeavoring to find out at first hand the cause of the symptoms of which the patient complains by starting at his head and going to his feet, using all of the methods of examination known to the diagnostician.

Malaria is the most common tropical disease, and, in temperate climates, the diagnosis of malaria is made on purely clinical evidence too many times. Some of the following cases show how erroneous this diagnosis may be when based on clinical evidence alone. The symptom complex of chill, fever, and sweat is common to many diseases, among them malaria. The shortest way to the diagnosis when the patient complains of these symptoms is to say that the condition is due to malaria and administer quinine. Modern methods have shown that the only proper way to arrive at a diagnosis of malaria, either acute or chronic, is after the demonstration of parasites in the peripheral blood. There be many men who have not yet accepted this method of arriving at a diagnosis of malaria and who still adhere to the old method of making a diagnosis on the clinical manifestations. Among the diseases that stimulate malaria in clinical manifestations are stricture of the urethra, abscess of the liver and other purulent collections about the liver, all septic processes, myocarditis, tuberculosis, syphilis and occasional cases of beginning leukemia.

One of the cases of quartan malaria and the case of estivoautumnal malaria were reported before this society at its meeting in 1909. (*New York Medical Journal*, July 8, 1909.) The other case of quartan malaria and the cases of benign tertian malaria showed nothing particularly interesting or unusual. Three cases of benign tertian infection and the case of quartan infection showed an increase in the large mononuclear leukocytes upon making a differential count: 23.4 per cent, 17.2 per cent, 11.4 per cent, 19.4 per cent. One of the cases of benign tertian malaria did not show an actual increase in the percentage of large mononuclear cells, 9.6 per cent being recorded. In one of the cases of benign tertian malaria the paroxysms occurred at 4 P. M., in one at 11:30 A. M. and in two the actual hour was not recorded, but in one of these the paroxysms occurred in the afternoon and in the other they occurred in the morning. In the case of quartan malaria the paroxysms occurred at 11:00 A. M. The histories of these cases follow:

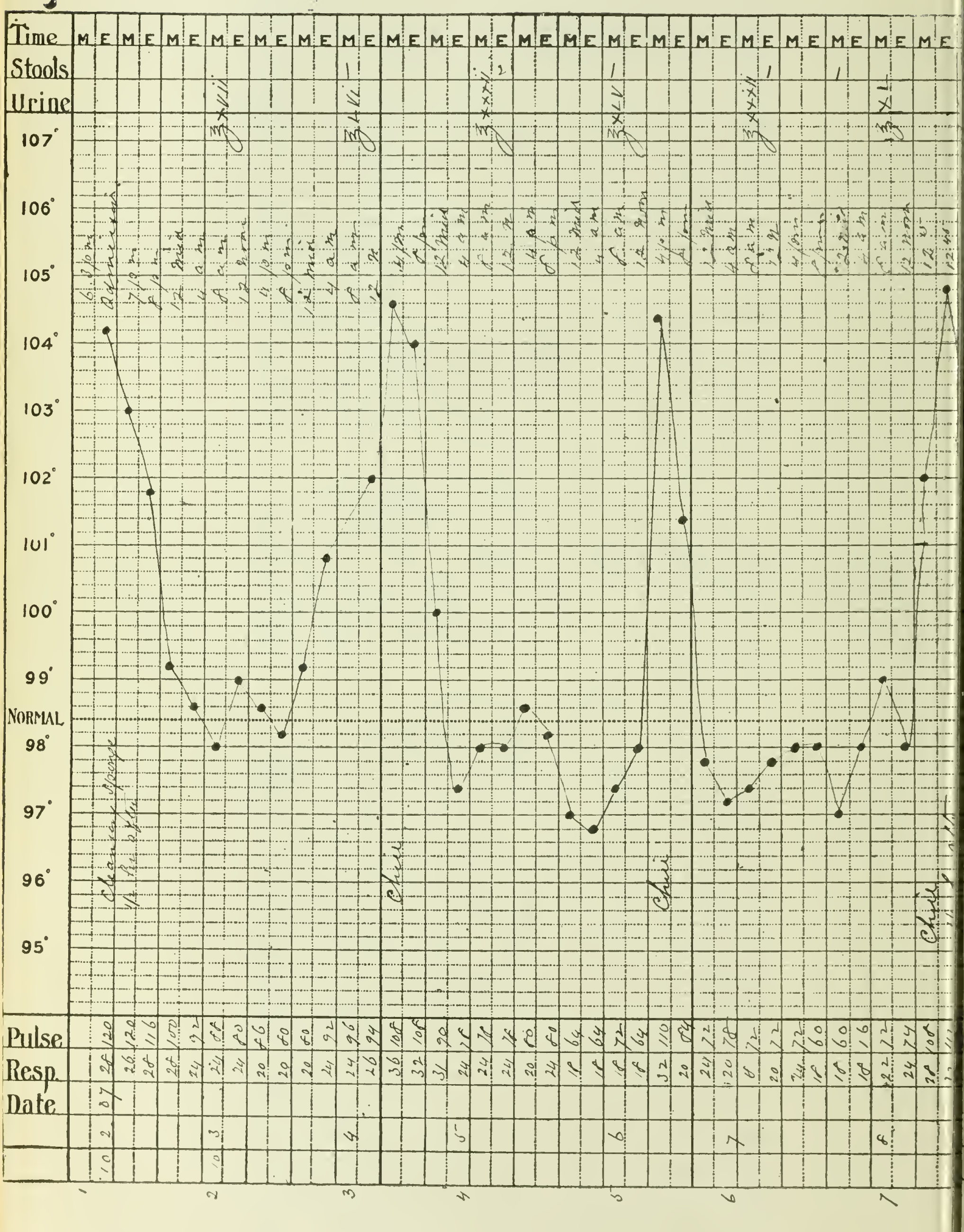
CASE I BENIGN TERTIAN MALARIA.

Male, white, aged 18 years, occupation factory hand, a native of Russia, was admitted to the hospital (No. 14687) in the service of Dr. A. A. Eshner, with a diagnosis of benign tertian malaria.

Family history: Negative.

Previous history: Negative.

Present trouble: For two months before the patient had complained of headache and chilly sensations. He had no distinct chills and no nose bleed. A few days before admission he began to complain of pain in his back and legs and the day before admission he had a distinct chill. On admission his temperature was 104 degrees, pulse 120, respiration 28. On the day after admission the temperature did not rise above 99 degrees, but on the following day it rose to 104.6 degrees, accompanied by a chill. On the day following that the highest temperature recorded was 98.6 degrees. The following day the temperature rose to 104.4 degrees, accompanied by a chill. On the following day the highest temperature recorded was 99 degrees. On the next day the temperature again rose to 104.8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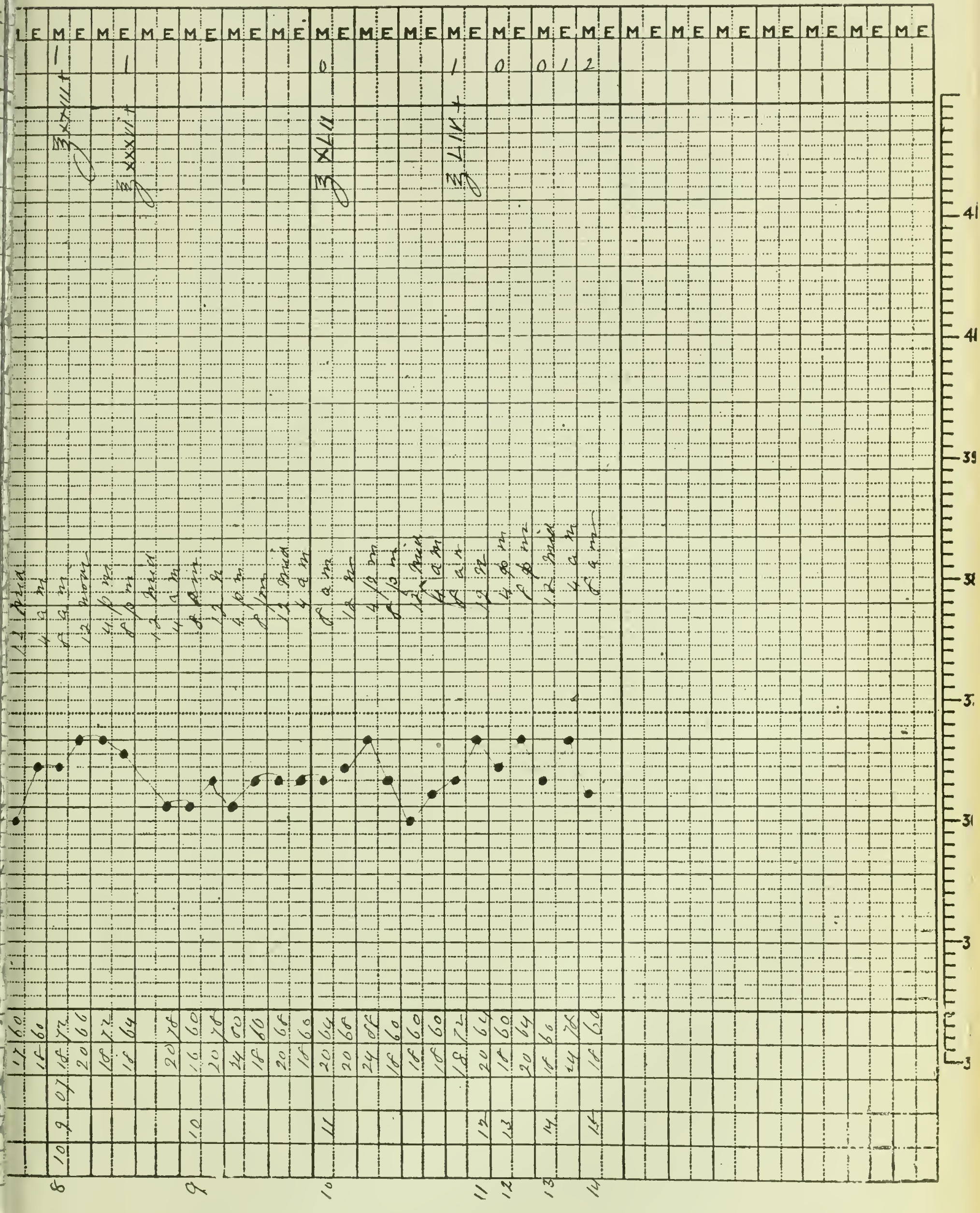
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degrees, accompanied by a chill. At the time of examination the blood count gave the following result:

Erythrocytes	5,050,000
Leukocytes	6,400
Ratio	1—780
Hemoglobin	Not taken
Differential count	
Polymorphonuclear neutrophiles	51.0 per cent
Lymphocytes	19.4 per cent
Large Mononuclears	23.4 per cent
Transitionals	3.4 per cent
Eosinophiles	2.4 per cent
Myelocytes	0.4 per cent
	100.0 per cent

Red cells slightly altered in size. Slight granular degeneration. In counting 100 leukocytes 18 tertian parasites were seen, chiefly half grown rings.

CASE 2.—BENIGN TERTIAN MALARIA.

Male, white, aged 29 years, occupation driver, native of New York, was admitted to the hospital (No. 14163) in the service of Dr. David Reisman, with a diagnosis of benign tertian malaria.

Family history: Negative.

Previous history: Negative.

Present trouble: For the past four years the patient had been working in Missouri. During this period his health has always been good, but in January, 1907, while working in a swamp where a good part of the time he had to stand in water, he had an attack of chills and fever. He never fully recovered from this attack and has had more or less chills and fever for weeks. At first the attacks came on every second or third day in the early afternoon. On admission to the hospital he complained of pain in the precordium, slight cought without expectoration, headache, vomiting and poor appetite. Examination of the urine gave the following results: Color, straw; reaction, alkaline; specific gravity, 1.010; no sediment, no albumen, no casts.

The blood examination gave the following results: Erythrocytes, 2,730,000; leukocytes, 17,000; ratio, 1,160; hemoglobin examination not made. Differential count:

Polymorphonuclear neutrophiles	73.6 per cent
Lymphocytes	7.8 per cent
Large Mononuclears	17.2 per cent
Transitionals	0.6 per cent
Eosinophiles	0.2 per cent
Basophiles	0.4 per cent
Myelocytes	0.2 per cent
	100.0 per cent

Forty-three malarial parasites were seen to ten leukocytes. Benign tertian rings and gametocytes. Schuffner's granules well marked.

The patient had three distinct malarial paroxysms while under treatment in the hospital, the maximum temperature being 104.8 degrees, 104.8 degrees and 106 degrees respectively. On the alternating days the patient had an abortive paroxysm, the temperature reaching 101 degrees and 102.8 degrees respectively. During the progress of the case the red blood corpuscle count rose progressively.

CASE 3.—BENIGN TERTIAN MALARIA.

Male, white, aged 23 years, occupation dishwasher. Was admitted to the hospital (13549) in the service of Dr. A. A. Eshner, with a diagnosis of malaria.

Family history: Negative.

Previous history: The patient was an Austrian. He had been in this country for five years. He had never had an attack similar to the one for which he was admitted. At the age of 14 he had an attack of pain in the left inguinal region from some unexplained cause. At the age of 18 he had an attack of fever which kept him in bed for three weeks. He had not felt well since that time, although he had never complained of any acute disease. During the past year he had lost 25 pounds in weight and had had night sweats occasionally.

Present trouble: For the past two months the patient had had a cough; at first the cough was very tight and troublesome, but lately it had been looser and not so troublesome. During this period the patient had had very severe chills followed by fever at irregular intervals, except the last three attacks, which occurred at intervals of four days. At one period he had four chills on each of four successive nights at 7 o'clock. During part of this time he was in Tennessee and Virginia where he took quinine. On the day of his admission to the hospital he had been in Philadelphia but a short time and had been complaining of chills ever since he reached the city. Upon admission his temperature was 105.2 degrees; pulse, 120; respiration, 24. The liver dullness extended from the fifth interspace to the eighth interspace; its edge was not palpable. The splenic dullness began at the seventh rib and extended to the eleventh rib; its edge was not palpable. Malarial parasites were found in the blood. The temperature dropped to normal in about fourteen hours and did not exceed the normal after that time during his stay in the hospital.

A blood examination made the day after admission gave the following result:

Erythrocytes	5,310,000
Leukocytes	9,600
Ratio	1—553
Hemoglobin, per cent	57
Color Index	0.55
Differential Count	
Polymorphonuclear neutrophiles	73.2 per cent
Lymphocytes	15.4 per cent
Large Mononuclears	9.6 per cent
Transitionals	1.0 per cent
Eosinophiles	0.4 per cent
Basophiles	0.4 per cent
	100.0 per cent

Numerous large and small tertian rings and gametocytes were seen; 177 parasites were seen in counting 100 leukocytes.

Here is a case of benign tertian malaria in which no increase of large mononuclear leukocytes is recorded. The infection was evidently of fairly long standing.

CASE 4.—BENIGN TERTIAN MALARIA.

Male, white, aged 23 years, occupation painter, was admitted to the hospital (11701) in the service of Dr. R. Max Goepp with a diagnosis of malaria.

Family history: Negative.

Previous history: Negative.

Present trouble: The patient was referred to the hospital wards complaining of headache, chills and constipation. During his stay in the ward he passed several adult ascaris lumbricoides worms. On admission his temperature was 101 degrees, pulse, 86; respirations, 26. The afternoon temperature on the day following admission was 99.4 degrees. The morning temperature on the following day was 100 degrees. The fourth day of his stay in the hospital his temperature was normal; the following day it rose to 100.6 degrees and on that day the blood examination showed benign tertian parasites and the following differential count:

Polymorphonuclear neutrophiles	77.0 per cent
Lymphocytes	10.4 per cent
Large Mononuclears	11.4 per cent
Transitionals	0.4 per cent
Eosinophiles	0.6 per cent
Basophiles	0.2 per cent
	100.0 per cent

CASE . —QUASTAN MALARIA.

Female, white, aged four years, was treated in the dispensary service of Dr. Samuel McC. Hamilton (No. 2235) for malaria.

Family history: Negative.

Previous history: The child was born in Naples and had come to the United States six weeks before she was first seen in the dispensary. She had had measles, whooping cough and what was called scarlet fever. With this disease the patient was sick for six weeks and she had had numerous attacks of fever since.

Present trouble: The patient complained of fever. She got a chill about 11 o'clock every third day which lasted for an hour. This was followed by fever which lasted about six hours, when the fever disappeared. During the attack of fever the child was yellowish. Upon making a physical examination the important points developed were that she had a sallow complexion and marked enlargement of the liver and spleen. Between the attacks of fever the child had a poor appetite and played but little. In the recumbent position the heart showed a well-marked late systolic murmur in the second and third interspaces, which was not heard in the upright position and which was not transmitted. The spleen extended two inches below the costal margin. The liver was palpable an inch and one-half below the costal margin. Examination of the blood made when the temperature was 104 degrees gave the following results:

Erythrocytes	6,700,000
Leukocytes	5,920
Ratio	1—1,131
Hemoglobin, per cent	68
Color Index	0.50
Differential count	
Polymorphonuclear neutrophiles	50.6 per cent
Lymphocytes	27.4 per cent
Large Mononuclears	19.4 per cent
Transitionals	0.8 per cent
Eosinophiles	1.2 per cent
Basophiles	0.4 per cent
Myelocytes	0.2 per cent
	100.0 per cent

In counting 500 leukocytes, 125 medium sized quartan rings were found.

CASE 6.—LATENT MALARIA.

Female, black, aged 28 years, occupation dressmaker, a native of Jamaica, was admitted to the hospital (14788) in the service of Dr. W. M. Sweet, with a diagnosis of cyclitis.

Family history: Negative.

Previous history: Two years before coming to the United States from Jamaica, while she was a resident of the island of Jamaica, she had malaria, but did not know what variety.

Present trouble: The patient thought she caught cold at the time of the earthquake in Jamaica. She complained of pain in the left eye, headache and fever. About two weeks after the beginning of the pain a film formed over the eye which obscured her vision. She frequently complained of backache. The eyeball was enucleated under aseptic conditions was amber in color; acid in reaction; 1.024 in specific gravity; presented a moderate amount during her stay in the hospital. The urine of sediment composed of leukocytes, uric acid crystals and amorphous urates. There was no albumen and no glucose. The feces were examined and one ascaris lumbricoides ovum was found. The blood examination gave the following result:

Erythrocytes	3,840,000
Leukocytes	7,600
Ratio	1—505
Hemoglobin, per cent	80
Color index	1.04
Differential count	
Polymorphonuclear neutrophiles	64.6 per cent
Lymphocytes	11.8 per cent
Large Mononuclears	17.4 per cent
Transitionals	4.0 per cent
Eosinophiles	2.2 per cent
	100.0 per cent

In counting 500 leukocytes, one cell, resembling a partially degenerated gametocyte, was seen.

The patient's temperature while in the hospital did not reach 100 degrees at any time.

In this case the fact that the patient was a native of Jamaica and had been in this country but a short time when she was admitted to the hospital for a distinct ophthalmological condition rendered the blood examination of interest. The examination showed a moderate reduction of the red cells, a slight reduction in the number of leukocytes, a high color index and a high large mononuclear percentage (17.4). During the enumeration of 500 leukocytes one cell resembling a partially degenerated gametocyte was seen. It would appear that this is a case of latent malaria, and it would also appear that under favorble conditions this patient might develop an acute attack of malarial fever of some kind.

CHILLS SIMULATING MALARIA CAUSED BY SEPTIC ABSORPTION.

Female, white, aged 38 years, occupation housewife, was a private patient (696) who was referred for a condition which she called "slow fever." At the time of making her first visit the patient complained of cold in the head with cough, chill, fever and muscular pains. She had had these symptoms for two or three days and they were gradually getting worse.

Family history: Negative.

Previous history: The patient was born in Louisiana. She went to the tropics twenty years ago and had her first attack of malaria about three weeks after her arrival. She had had two or three other distinct attacks. She had two attacks of hemoglobinuric fever, apparently without immediately antecedent malarial infection; both attacks were cured during treatment with quinine. She had a distinct attack of dengue. She had not had dysentery nor yellow fever.

For three years she had had what she called "slow fever." The temperature would be from 99 to 100 degrees every day. The attacks of "slow fever" would last about three weeks, then there would be an interval of three weeks or longer when she would be without febrile manifestations. One attack lasted for three months. This condition was not accompanied by chills. The febrile attack would come on at about nine or ten o'clock in the morning and would last nearly all day; sometimes it would be accompanied by sweating. There was no cough except a dry, hacking cough, which was apparently due to throat trouble. She had had dyspeptic symptoms during all the time that she had had the "slow fever." She had had probably twelve attacks of influenza. The dyspeptic symptoms included nausea, usually without vomiting. The bowels were inclined to be loose and moved two or three times a day for a year. Following that she was constipated for a while; the attacks of constipation alternating with regular bowel movements. Sometimes she complained of pain in the upper quadrants, but no pain in the lower quadrants of the abdomen. There was no distension; there was some belching and some flatus. The stools were usually brown in color and contained considerable mucus, which occurred in long strings. On some occasions, particularly when constipated, the patient passed blood on account of the existence of hemorrhoids. She had no headache. She had a bad taste in her mouth all the time and had had a chronic nasopharyngitis for eleven years. Dyspnea and palpitation of the heart on exertion were noted. There was no edema, no vertigo. The appetite was good and thère were no genito-urinary symptoms. The menstrual function was regular.

Physical Examination.—A rather slight, white, adult female. Apparent age 40 years. Hair light brown, fairly abundant.

Pupils normal, reacted promptly to light and distance. Conjunctivae slightly injected.

The tongue was clean and moist. The throat was red and dry. The tonsils were not swollen.

The chest was long and narrow and rather thin; the intercostal angle was acute. At the right apex both anteriorly and posteriorly there were high-pitched percussion note, prolonged expiration, and increased vocal resonance with numerous moist rales at the end of inspiration. Examination of the heart showed no pathological signs.

Abdomen: The abdomen was not distended. There was some tenderness over the appendix and some over the gall bladder. Neither the spleen nor the liver were enlarged. There was no tumor. The patient was slightly anemic.

Examination of the blood:

Erythrocytes	5,200,000
Leukocytes	8,604
Ratio	1-601
Hemoglobin (Fleischl), per cent.	86
Color index	0.75

Differential count:

Polymorphonuclear neutrophiles	76.8 per cent
Lymphocytes	10.2 per cent
Large Mononuclears	9.4 per cent
Transitionals	2.8 per cent

Eosinophiles	0.8 per cent
	100.0 per cent

No malarial parasites were seen.

Examination of the urine showed: Color, amber; specific gravity, 1,017; considerable cloudy sediment composed of bladder and vaginal epithelium, bacteria, and leukocytes. Chemically albumin was present, but there were no casts.

Examination of the stools showed neither ova, embryos, adult parasites nor protozoa.

The sputum contained an almost pure culture of a gram-positive diplococcus. The ophthalmotuberculin test was positive.

On February 19, 1908, and on February 21, 1908, following exposure in a sleet storm, the patient had a chill followed by fever and sweat. Examination of the blood on February 22, at 11 a. m., showed numerous large benign tertian rings. A cell count was not made, but the differential count gave the following results:

Polymorphonuclear neutrophiles	57.6 per cent
Lymphocytes	6.6 per cent
Large Mononuclears	26.8 per cent
Transitionals	6.4 per cent
Eosinophiles	2.0 per cent
Basophiles	0.4 per cent
Myelocytes	0.2 per cent
	100.0 per cent

Sixty-nine benign tertian parasites were seen in counting 500 leukocytes. On March 7 a second differential count was made with the following results:

Polymorphonuclear neutrophiles	74.4 per cent
Lymphocytes	8.8 per cent
Large Mononuclears	14.4 per cent
Transitionals	1.6 per cent
Eosinophiles	0.2 per cent
Basophiles	0.4 per cent
Myelocytes	0.2 per cent
	100.0 per cent

No malarial parasites were seen.

In this case we have the presence of two distinct diseases. When the patient was first seen the symptoms could easily be accounted for by the existence of the tuberculous consolidation at the apex of the right lung, which was quite sufficient to account for the attacks of "slow fever," which were thought to be due to some irregular form of malaria. At this period of the case the blood examination showed no indication of a previous malarial infection, or of latent malaria. There were no parasites in the peripheral blood and the differential leukocyte count, while it showed a rather high normal mononuclear percentage (9.4), was not of such a character as to lead to a suspicion of even latent malaria. The confirmatory result of the ophthalmo-tuberculin reaction was sufficient evidence to establish the diagnosis of chronic pulmonary tuberculosis. The attack of malaria developed following exposure to cold. The patient on a night in February, when the weather was warm and muddy, went to the theater with a light wrap about her. While in the theater the temperature suddenly fell and a sleet storm developed in which she had to return home. As a result of this exposure a distinct malarial attack followed, which was shown by the presence of parasites in the peripheral blood and the rise in the large mononuclear percentage from 9.4 to 26.8. Two weeks later the parasites had disappeared from the peripheral blood and the large mononuclear percentage had fallen to 14.4.

CASE 8. SEPSIS.

Female, white, aged 26 years, occupation housewife, presented a laceration of the cervix uteri and of the perineum.

Family history: Negative.

Previous history: The patient had had an attack of anemia when she was 16 years old.

Present trouble: Six months after the birth of her first child, about three years before, the patient began to complain of pain in the back and the left side of the chest. She complained of frequent urination and of nocturnal urination. The urine burned, but there was no record of a vaginal discharge. The patient had had two subsequent normal pregnancies and labors, during which the above symptoms increased. An examination showed an extensive laceration of the perineum, laceration of the cervix uteri, and a cystocele. These lesions were operated upon in the ordinary way, and two days after the operation the patient's temperature rose to 101.8 degrees. The packing was removed, a mercury bichloride douche was given, and the next day the temperature fluctuated at about 100 degrees. The following day, however, it again rose to 103.4 degrees, and on that day the patient had a good-sized hemorrhage from the vagina. At 8 p. m. that day the patient's temperature was 104 degrees, following a chill which occurred at about 11:30 a. m. The attending physician suspected malaria and had an examination for malarial parasites made with the following result:

Polymorphonuclear neutrophiles	73.2 per cent
Lymphocytes	13.0 per cent
Large Mononuclears	9.6 per cent
Transitionals	1.8 per cent
Eosinophiles	2.4 per cent
	100.0 per cent

No malarial parasites were found.

The temperature kept up an irregular course for five days longer, during which time the agglutination test for typhoid fever was negative, and a second examination for malarial parasites gave the following result:

Polymorphonuclear neutrophiles	80.8 per cent
Lymphocytes	13.6 per cent
Large Mononuclears	2.6 per cent
Transitionals	1.8 per cent
Eosinophiles	0.4 per cent
Basophiles	0.8 per cent
	100.0 per cent

No malarial parasites were found, but one normoblast was seen in counting 500 leukocytes. In spite of the results of this blood examination the attending physician made a diagnosis of malaria because the patient had an irregular temperature and gave a history of "malaria" a few months before. The temperature returned to normal and the patient subsequently made an uninterrupted recovery.

This is evidently a case of septic absorption from the field of observation. The symptoms coming on two days after the operation, accompanied by hemorrhage; the increase of polymorphonuclear leukocytes and the absence of malarial parasites point unmistakably to this conclusion.

CASE 9. TUBERCULOUS PERITONITIS.

Male, white, aged 5 years, was admitted to the hospital (17029) in the service of Dr. James H. McKee, with a diagnosis of pneumonia.

Family history: Negative.

Previous history: The child was born at term after a normal labor. He was breast-fed for one month and was then fed on condensed milk. He had been a healthy child and was well developed. He had had measles and chickenpox, but not scarlet fever, diphtheria, whooping cough or mumps.

Present trouble: A few days before admission the child was noticed to be drowsy and dull. The following day he was worse, and his mother said that his body felt hot. On that day he vomited a good deal. His bowels were loose and the stools resembled a soft boiled egg in appearance. He complained of headache, pain in the back and chest pain, which was made worse by coughing. He was delirious and restless during the night. On admission the temperature was 102 degrees; the abdomen was much distended, but was not very tense.

Physical examination (made by Dr. McKee). McEwen's sign was suspicious and bilateral. The eyelashes contained the ova of pediculi; the tongue was moist and slightly coated. There was a general enlargement of the superficial lymph nodes; the axillary nodes were small; the inguinal nodes were small. There was a large scar at the level of the left nipple, probably the result of a burn. There was a delayed tache on the chest and abdomen. There was no abnormality discovered in chest either on inspection or palpation. The breathing was of the abdominal type. On the outer half of the supraclavicular fossa there was absolute dullness. The liver extended 2½ inches below the costal margin. The spleen was very much enlarged and hard and extended 2½ inches below the costal margin; its notch was easily felt. The upper border of the spleen reached to the fifth rib. There were no typhoid spots. There was dullness in both flanks with slight fluctuation. In the upper portion of the right chest the expiration was prolonged and blowing and numerous rales were heard, while subcrepitant rales were audible over the entire chest. The patient had an irregular temperature, rising on some occasions as high as 106 degrees, and dropping on other occasions to 98.6 degrees. On account of the distended abdomen and irregular temperature and the pulmonary signs, a diagnosis of tuberculous peritonitis was made. Dr. Francis T. Stewart opened the abdomen and removed a small amount of clear ascitic fluid. Examination of the abdominal viscera, however, showed no visible tubercles. The mesenteric lymphnodes and the spleen were both seen to be enlarged, and one of the mesenteric nodes was removed for histological examination. In the report received from Dr. James A. Kelly, a diagnosis of acute inflammation was made. The cellular elements of the lymphnode were hyperplastic and many areas of necrosis were seen scattered through the tissue. The tissue was stained for tubercle bacilli, but none were found. The fluid removed from the peritoneal cavity at the operation was examined for the presence of tubercle bacilli, but none was found. Cultures made from the fluid were sterile at the end of twenty-four hours. Examination of the blood gave the following results:

Erythrocytes	4,120,000
Leukocytes	12,000
Ratio	1-323
Hemoglboin (Fleischl), per cent.	66
Color index	0 80

Differential count:

Polymorphonuclear neutrophiles	57.6 per cent
Lymphocytes	33.2 per cent

Large Mononuclears	7.8 per cent
Transitionals	0.6 per cent
Myelocytes	0.8 per cent
	100.0 per cent

No malarial parasites were seen.

In this case the suspicion of the existence of malaria was brought about by the facts that the child had a high temperature with marked remissions and that the spleen was very much enlarged and hard. There were few, if any, chills. Examination of the blood showed, in the first place, no malarial parasites; in the second place a leukocytosis, 12,000; and in the third place, an increase of the lymphocyte percentage, and a large mononuclear percentage which while high (7.8), was within the normal limits. The distension of the abdomen, irregularity of the temperature curve, and the signs of consolidation of the lung led to the diagnosis of tuberculous peritonitis, which proved upon operation to be correct. The original diagnosis of pneumonia was correct as indicated by the physical signs.

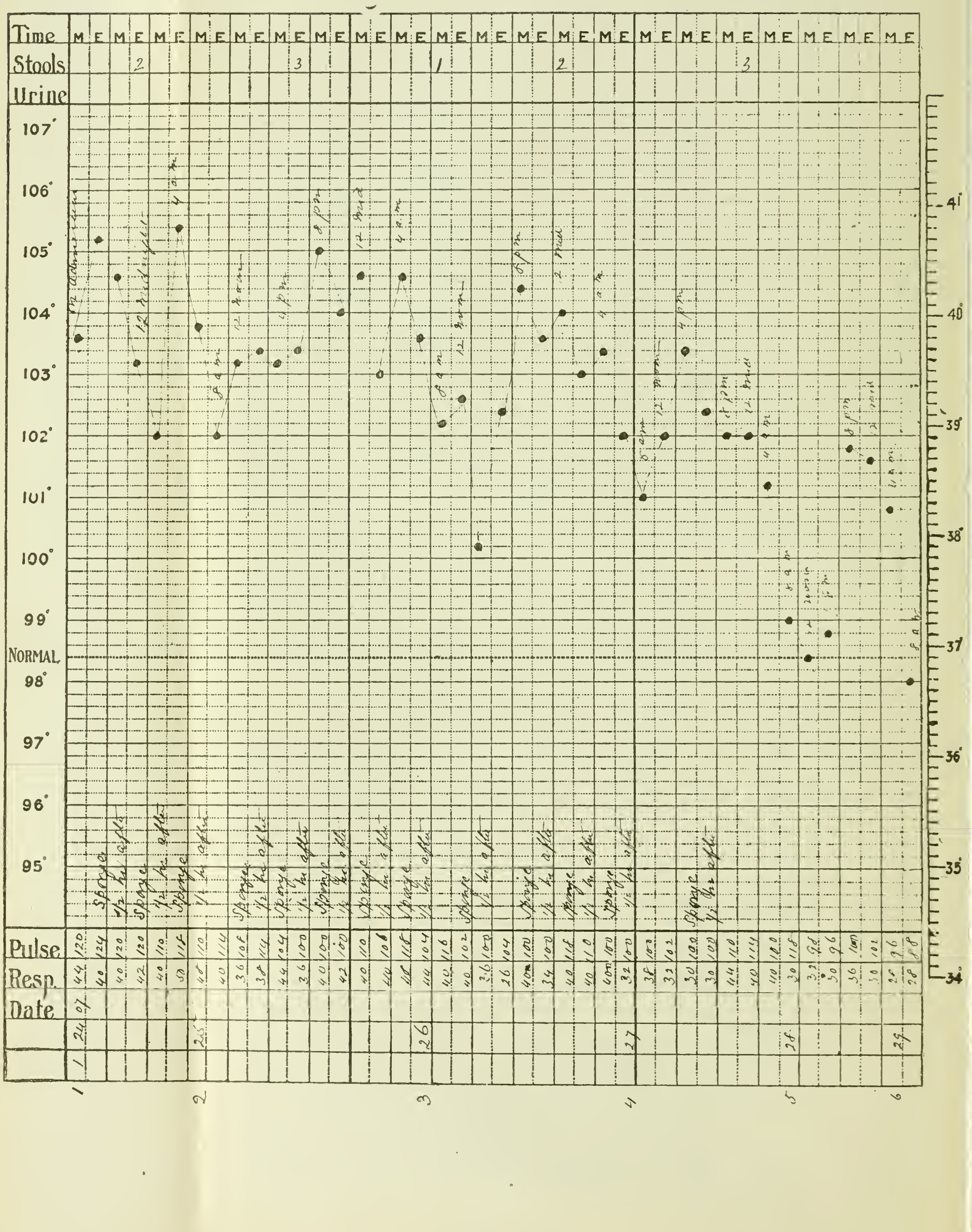
CASE 10. CEREBRAL ABSCESS.

Male, white, aged 28 years, occupation laborer, native of Italy, was admitted to the hospital (13736) in the service of Dr. A. A. Eshner with a diagnosis of cholecystitis.

Family history: Negative.

Previous history: Negative.

Present trouble: The condition for which the patient was admitted to the hospital began in January, 1907. For two months before that he had been languid and complained of pain in his back, legs and head. He also had some pain and tenderness all over the abdomen. Both the spleen and the liver were enlarged and tender, and the patient had some cough and was decidedly jaundiced. A urine examination made at this time showed albumin and a very large number of granular casts, with pus and epithelial cells. Bile was present and a positive diazo reaction was obtained. The temperature on admission was 103.6 degrees, pulse 120, respirations 44. The next morning the temperature registered 105.2 degrees,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pulse 124, respirations 40. For the next six days the temperature ran an irregular course, the maximum being 105.4 degrees and the minimum being 98 degrees. During this period a blood examination was made for the presence of malarial parasites. The leukocyte count, made by the resident physician, showed 9,000 white cells to the cubic millimeter of blood. No malarial parasites were seen. The differential count gave the following result:

Polymorphonuclear neutrophiles	72.2 per cent
Lymphocytes	12.8 per cent
Large Mononuclears	14.8 per cent
Transitionals	0.2 per cent
	100.0 per cent

A diagnosis of pneumonia at the apex of the left lung was made during this period. During the following six days, that is from January 30 to February 5, the temperature showed considerable fluctuation, the maximum 100.8 degrees, and the minimum 97 degrees. During this period the following notes were made by Dr. David Riesman, who assumed charge of the wards on the first day of February: "The patient seems to be in much distress. He has a hacking cough, with scanty expectoration, and a slight purulent discharge from the right ear. Chest well formed, rather broad below, with much enlargement of the veins in the right hypochondriac region. There is a depression above the left clavicle and slightly diminished expansion below. At the left apex, above the clavicle, and in the first and third interspaces, there is impaired resonance, with harsh inspiration, prolonged expiration and numerous subcrepitant and coarse sonorous rales. These rales are heard not only at the apex, but all over the left side of the chest. Occasional rales can be heard in the right side of the chest. The other portions of the chest show hyperresonance on percussion except in the right supraspinous fossa, where there is impaired resonance.

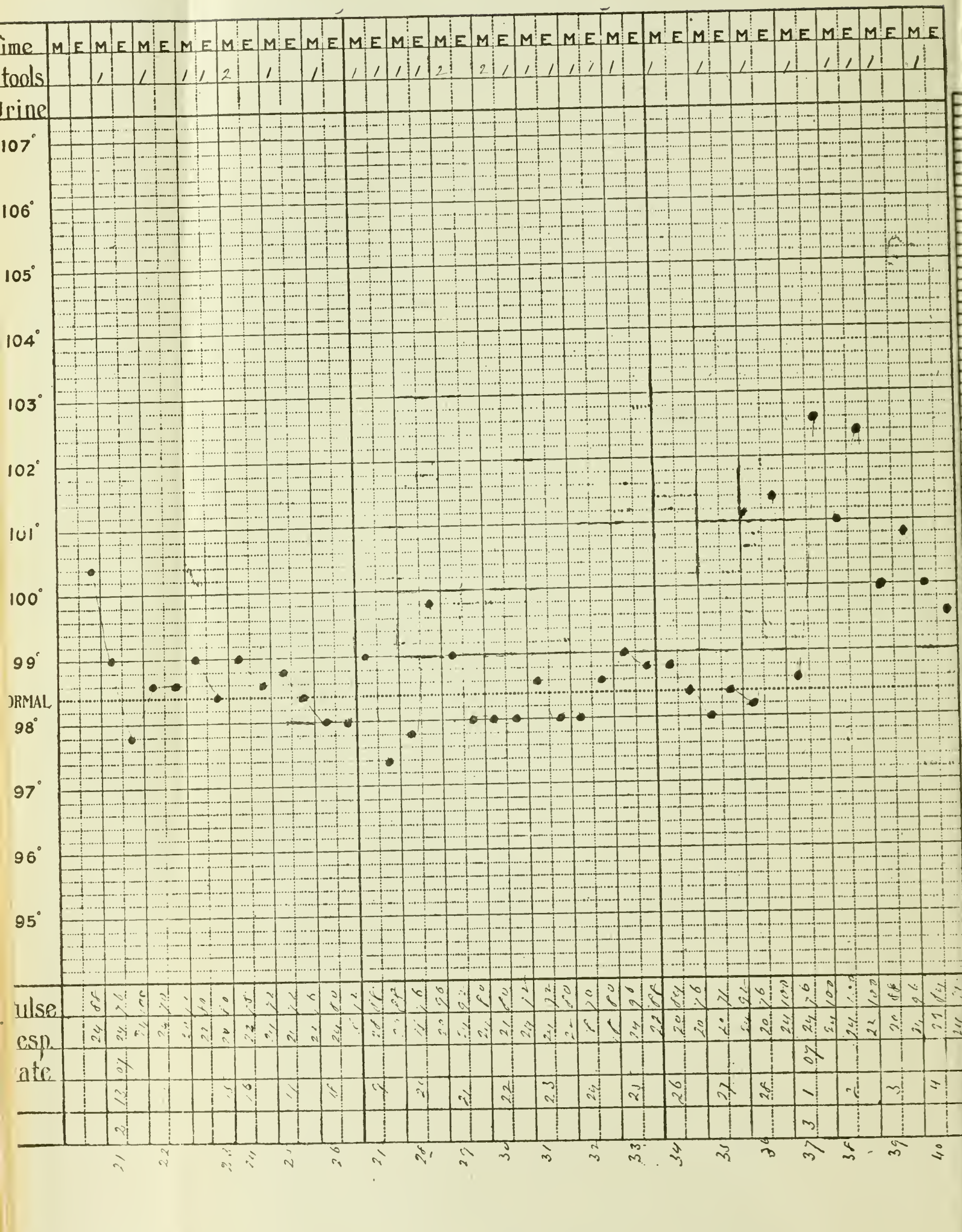
"Heart: The area of cardiac dullness is

diminished by the emphysematous lungs. The heart sounds are feeble, short and slow.

"Abdomen: The abdomen is distended. There is slight dullness in the right flank, but elsewhere the percussion note is tympanitic. There is no increased sense of resistance. The liver dullness extends from the sixth interspace to two fingers' breadth below the costal margin. The spleen is palpable."

Dr. Riesman made a diagnosis at this time of tuberculosis of the upper lobe of the left lung. For the following two days the patient had a normal temperature; that is to say, February 5 and 6. On February 7, at 10 o'clock in the morning, the patient had an epileptiform convulsion, which lasted about three minutes, during which he bit his tongue. The patient had seven other similar convulsions between the time of the first and 8 o'clock in the evening. In the afternoon at 4 o'clock the temperature rose to 102.8 degrees, but it had fallen to normal by 8 o'clock the following morning. For the next nineteen days his temperature hovered about the normal line with an occasional rise to 100 degrees. During this period numerous physical examinations were made and urinary examinations were made from time to time which resulted in practically the same findings as those already recorded. Toward the end of this period the patient's cough had disappeared, the convulsions had ceased, the consolidation of the left lung had cleared up to some extent. By the second of March, under treatment by Dr. Walter Roberts, the discharge from the ears had ceased but the patient complained of headache, particularly in the left temporal region. From the 2d to the 8th of March there was a marked remittent temperature, the thermometer registering as high as 102.6 degrees and falling between two and three degres. At this time Dr. Camp, from the clinic of Professor Spiller, made a diagnosis of cerebral abscess. The patient was stuporous and somewhat aphasic. He had right-sided facial paralysis, marked nystagmus in both eyes, and paresis of the right leg. In closing his eyes the patient's right lids did not approximate entirely and he would not protrude his tongue. The sensation seemed good in the face. During the progress of one of the examinations he had an epileptiform convulsion. Dr. Walter Roberts examined the ears and found the left external auditory canal filled with yellowish pus, with no swelling or tenderness over the mastoid. At 6 o'clock in the evening the patient had another convulsion. The following day an ophthologic examination by Dr. Schneideman resulted negatively. On the 12th of March Dr. John B. Roberts trephined the skull and evacuated an abscess containing about three drams of pus from the temporal lobe of the brain. Following the operation the temperature rose to 103.6 degrees, and in a little more than twenty-four hours fell to subnormal, to rise again at the end of the next twenty-four hours to 103.4 degrees. After that there was continued fever, with remissions of one or two degrees until the patient died. Following the operation the patient began to have sweats, and a second examination of the blood for malarial parasites was made with a negative result. At this time, however, no differential count was made. The pus evacuated from the abscess in the temporal lobe of the brain was examined by Dr. James A. Kelly and showed pneumococci and streptococci. Five days after admission agglutination tests were made with bacillus typhosus and bacillus paratyphosos, both with negative results. The patient died, but no autopsy was permitted.

In this case a positive diagnosis cannot be made. The history and the differential leukocyte count both point toward a recent malarial infection. The history shows a periodic recurrence of chill, fever and sweat every other day, although the patient was of the opinion that occasionally he had his attacks every third day. The differential leukocyte count on admission gave 29.6 per cent of large mononuclear leukocytes, but no mala-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rial parasites were found nor were pigmented leukocytes discovered. The second blood examination, which was made fifteen days later, showed the persistence of the high large mononuclear percentage. Against the interpretation of this case as one of recent malaria, the following facts have to be considered: First, the irregularity of the chill, fever and sweat symptom-complex, according to the history. The patient was not sure, but thought he had some of his attacks every third day instead of every other day. Second, the fact that the liver and the spleen were both normal in size, and that the cervical lymphnodes were enlarged on one side. Third, the absence of pigmented leukocytes in the blood. Fourth, the presence of a slight leukocytosis, 11,000 on the first examination, 12,000 on the second. By examining the temperature chart it will be found that the attacks of fever during his stay in the hospital occurred at 8 p. m. on October 31, at midnight on November 5, at 3 a. m. on November 9, at 8 p. m. on November 9, and at midnight on November 14. The second paroxysm followed the first in five days, the third followed the second in four days, the fourth occurred on the same day as the third, and the fifth followed the fourth in five days. There is more evidence against this case being one of malaria than there is in favor of its being one of malaria. I am of the opinion that such a case as this one ought not to be unqualifiedly put down to be an example of malarial infection.

CASE. PULMONARY TUBERCULOSIS AND BENIGN TERTIAN MALARIA.

This case is of considerable interest on account of the characteristics of the temperature curve and the slowness with which the symptoms developed. At the time of the patient's admission he had a continued fever with remissions of about three degrees. His spleen and liver were both enlarged, were both tender, and the blood count made at that time showed 9,000 leukocytes, 14.8 per cent of which were large mononuclears; 1,332 large mononuclears to the cubic millimeter of blood. No malarial parasites were seen, however. The physical examination showed a distinct pulmonary consolidation which was thought to be tuberculous. The absence of malarial parasites from the peripheral blood led to the opinion that malaria was not a part of the clinical picture. The patient had a discharging ear which developed a short time after his admission to the hospital and two weeks after his admission he had a tonic convulsion at ten o'clock in the morning which lasted about three minutes. During the remainder of the day he had seven other similar convulsions, The convulsions were not followed by paralysis. The knee jerks were not exaggerated; there was no ankle clonus and the Babinsky sign was absent. Still later a discharge from the opposite ear was discovered and a few days after that the discharge had ceased from both ears. On the 8th of March the patient had been complaining of headache for several days and an examination appeared to show that the spleen had diminished in size, although it was still palpable and tender, and that the liver was still enlarged and tender. The superficial lymph-nodes were also enlarged. At this time Dr. Camp, of Professor Spiller's clinic, made a diagnosis of cerebral abscess. The patient was operated on and a cerebral abscess containing about three drams of pus was evacuated. At about this time the patient had chills, his temperature was constantly above the normal line, ranging between 100 degrees and 102 degrees, pulse very rapid, and respirations increased in frequency; and a second examination failed to show malarial parasites. The chills were evidently due to septic absorption either from the track of the cerebral abscess or from an undiscovered and unevacuated abscess. A differential count was made only shortly after admission and not at the time of the second examination for malarial parasites.

We are not warranted in assuming that malaria had anything to do with the illness from which this patient was suffering at the time he was admitted to the hospital or subsequently. Although the man was a native of Italy, there was no definite history of malaria. At the same time the chronic enlargement of the liver and spleen, with some jaundice, might very readily be assigned to a previous malarial infection, and the increase in the large mononuclear leukocytes (14.8%) might be dependent upon that circumstance, but this does not mean that malaria was not in any way responsible for the pathological conditions found during the patient's last illness. It is possible that, had an autopsy been permitted, malarial pigment would have been discovered in the spleen or the liver.

CASE II. SPLENOMEGALY.

Female, white, aged about 40 years, occupation housewife. Was admitted to the hospital (13316) in the service of Dr. B. F. Baer with a diagnosis of chronic splenic tumor.

Family history: Negative.

Previous history: Negative.

Present trouble: Four years before the patient was first seen, she noticed a sudden enlargement of the abdomen with much pain and tenderness in the left side. The pain and tenderness were not constant. The conjunctivae were yellowish. There was some ascites but no edema of the legs. The liver was enlarged and palpable on deep pressure, its edge was hard and firm, but not tender. An examination of the blood made four days after admission gave the following results:

Erythrocytes	5,270,000
Leukocytes	12,400
Ratio	1—425
Hemoglobin, per cent	86
Color Index	0.81

Differential count:

Polymorphonuclear neutrophiles	74.4 per cent
Lymphocytes	12.0 per cent
Transitionals	11.4 per cent
Eosinophiles	2.0 per cent

Basophiles	0.2 per cent
	100.0 per cent

No malarial parasites were found. A second examination was made about five weeks later with the following result:

Erythrocytes	4,810,000
Leukocytes	4,000
Ratio	1—1202
Hemoglobin, per cent	78
Color Index	0.81

Differential count.

Polymorphonuclear neutrophiles	70.0 per cent
Lymphocytes	5.8 per cent
Transitionals	19.4 per cent
Eosinophiles	3.6 per cent
Basophiles	1.2 per cent
	100.0 per cent

No malarial parasites were found.

This case is one in which it has been impossible to arrive at a complete diagnosis. The patient was admitted for chronic splenic tumor. A large liver was associated with the enlarged spleen. The question at issue was whether the case was one of chronic malaria, myeloid leukemia, or splenic anemia. The original blood examination immediately excluded myeloid leukemia. The same blood examination would tend to discredit the view that the case was one of splenic anemia, on account of the leukocytosis, although the large percentage of transitionals (11.4) would seem to point to that condition. The second blood examination made five weeks after the first which showed a leukopenia (4000), a moderate degree of chloroanemia (color index 0.81) and a further increase in the percentage of transitional leukocytes (19.4) would seem to point to this condition. The question of the relation of a possible previous malarial infection to this case is interesting and one that can never be definitely determined. The patient could not recall ever having had acute malaria. She was a native of Italy, however, and it is well within the range of possibility that at some time during her life in that country she had had a malarial infection. If we are to consider that an increase of large mononuclear and transitional cells is positive indication of previous malarial infection, as some writers would have us do, we would necessarily conclude that this case was dependent upon a previous malarial infection, but it is now well known that other conditions may be accompanied by an increase in these cells. Personally, I am inclined to lay little stress upon such an increase as indicative of previous malarial disease and am inclined to look upon this case as one of beginning splenic anemia and not one of chronic malaria.

CASE 12. MYOCARDITIS.

Female, white, aged 37 years, occupation housewife and lecturer on missionary subjects; was a private patient (660) who presented herself with a diagnosis of chronic malaria.

Family history: Negative.

Previous history: The patient had had the usual diseases of childhood, including scarlet fever. She was married at the age of 22, and went to India with her husband, who was a missionary in Assam, in 1892. She remained in India until 1900, when she came home and remained for three years. She returned to India in the autumn of 1903, and remained on the field for a year and a half. In June, 1905, she returned to the United States. On her arrival in India, in 1892, she weighed 111½ pounds. Four months after her arrival in India she had an attack of malaria. This attack lasted, with intermissions, fairly continuously until she returned to the United States in 1900, except during the time that she was pregnant eleven years ago. She had one miscarriage at seven months, which was brought on by an attack of fever and lack of medical attention. She had had no diarrhea. She had complained of some difficulty in holding the urine in the morning,

Present trouble: The patient complained of irregular attacks of fever of varying length without definite periodicity. These attacks dated from her return to the United States in 1905 on account of poor health. Whenever the weather was warm and damp she had fever and when the weather cleared and the atmosphere was dry the attacks disappeared. She might have one attack in a month, one in two months, two in a month, etc. The attacks of fever came on slowly and for a week or less before the fever developed she was more sleepy than usual. She complained of lassitude and of general malaise with a chilly feeling. She had had no distinct chill during any of these attacks in the last two years. The thermometer had registered 101 degrees. The febrile attacks usually occurred between 11 a. m. and 3 p. m. She complained of cyanosis of the fingers and lips. There was no headache, no interference with vision, no sore throat, no nasal discharge, no cough, no expectoration, no chest pain, There was slight dyspnea on exertion; palpitation of the heart, but no vertigo; slight nausea, but no vomiting. No abdominal pain or tenderness. The bowels moved daily. The stools were semi-solid, brown, contained no blood and no mucus. The menstruation was regular, lasted five days, and was painful on the day before or on the first half day of the flow. There was no edema except a slight puffiness of the hands and fingers with numbness. No suborbital edema. The patient slept poorly. Her appetite was only fair. There was a tremor in the head and hands, no goiter, no exophthalmos.

Physical examination: The pupils were normal and reacted to light and distance. The conjunctivae were slightly pale and the sclerotics bluish.

The tongue was slightly coated; the teeth were well cared for; the mucous membrane of the mouth was pale; the throat was a little red; the complexion was sallow; the pulse was 64 per minute, dropped about every third beat and showed a tendency to dicrotism; temperature 99.20. The chest was long and narrow; the intercostal angle was acute.

Examination of the lungs showed no pathological signs.

Heart: The apex beat was neither visible nor palpable. The sounds were heard best in the normal position. There were no murmurs. The heart dropped every other beat. The muscular quality of the systolic sound was poor. The abdomen showed no pathological signs. The liver dullness extended from the sixth rib to the costal margin; the edge was palpable on deep inspiration. The splenic dullness was not obtainable on account of distension of the colon; its edge was not palpable. There was no ulceration in the nose. An examination of the blood gave the following result:

Erythrocytes	4,730,000
Leukocytes	8,000
Ratio	1—5914
Hemoglobin, per cent (Fleischl)	93
Color Index	0.98x

Differential count.

Polymorphonuclear neutrophiles	59.8 per cent
Lymphocytes	24.8 per cent
Large Mononuclears	10.4 per cent
Transitionals	3.2 per cent
Eosinophiles	1.8 per cent
	100.0 per cent

No malarial parasites nor pigmented leukocytes found.

Examination of the urine gave the following results. Color, pale amber; reaction, acid; specific gravity, 1016; considerable cloudy sediment composed of leukocytes, epithelium, mucus, and micro-organisms. There was a trace of albumen, but no glucose.

Examination of the feces gave the following result: Neither ova, embryos, adult parasites or protozoa present.

This is an interesting case. The patient had been treated for a considerable time by numerous physicians as one of chronic malaria. The only disease that could be demonstrated upon physical examination was a myocarditis. The examination of the blood showed a picture that was distinctly not that due to present or past malarial infection. The symptoms were relieved by treatment directed toward the improvement of the myocardium.

CASE 13. STRICTURE OF THE URETHRA.

White, male, aged 26 years, by occupation a student; was a private patient (658) who complained of chill, fever and sweat. The patient was first seen about nine o'clock p. m. when his temperature was 105 degrees, pulse 120. The family history was negative. He had had a similar attack of chill, fever and sweat the day before he was first seen. The patient had not been sick for several years, except for an attack of gonorrhea one year previously. The morning following the attack of chill, fever and sweat in which he was first seen, the patient's temperature was 98.4 degrees and pulse 76. He felt tired and weak and had not slept well. The patient was a native of Mexico, and an examination of the blood was made with the idea that the attack might be due to malaria. A cell count was not made but the differential count gave the following results:

Polymorphonuclear neutrophiles	72.5 per cent
Lymphocytes	18.0 per cent
Large Mononuclears	4.5 per cent
Transitionals	4.5 per cent
Eosinophiles	0.5 per cent
	100.0 per cent

No malarial parasites were seen.

An examination of a specimen of blood taken at night failed to show filaria embryos.

Two days after the first attack the patient was again seen with an attack of chill followed by fever and sweating. He had eaten pork for dinner. The chill began at 10:30 p. m., and while he was having the chill he vomited. At 1.30 a. m. the patient's temperature was 106.4 degrees, pulse 124. A soft systolic murmur was heard at the base of the heart which was not transmitted. There was harsh breathing at the base of the lungs. There was no enlargement of the spleen. The patient was perfectly conscious. At 10 a. m. the following day the temperature was 98.4 degrees, pulse 82. The patient was perspiring slightly and showed no pathological signs. Seven days after this attack the patient had another attack of chill, fever and sweat which began at one o'clock in the morning. His temperature was not taken. An examination of the urine at this time showed a large amount of pus, mucus and bladder epithelium. The color of the specimen was amber; its reaction acid, and it had a specific gravity of 1.017. There was no albumin and no glucose. The patient was referred to Dr. Edwin Martin, who, with considerable difficulty, succeeded in passing a filiform bougie into the bladder. The prostate gland was uniformly enlarged but there was no area of softening. There was a stricture of the urethra 2 3-4 inches from the external urinary meatus which would not allow a No. 23 bougie a boule to pass. A No. 16 would pass this stricture, accompanied by much pain; but it would not enter the bladder. The bladder could only be entered, as above stated, with a filiform. Dr. Martin, under ether anesthetization, performed a combined external and internal urethrotomy. Following this operation the patient had no recurrence of his chill, fever and sweat.

This is plainly a case of a symptom complex resembling that of malaria which is dependent entirely upon septic absorption from a stricture at the bulbomembranous junction.

CASE 14. EMPYEMA OF THE GALL BLADDER.

White, male, aged 55 years, occupation farmer, birthplace Russia; was admitted to the hospital (15101) in the service of Dr. A. A. Eshner with a diagnosis of malaria. The patient was a resident of New Jersey.

Family history: Negative.

Previous history: Thirty years ago while he was living in Russia the patient had malaria; otherwise he had always been strong and healthy up to his present illness, except for an attack of smallpox during childhood.

Present illness: For five weeks the patient had been complaining of pain in the lower right quadrant of his abdomen. The onset was sudden and in the afternoon of the day in which the pain began he had a chill which lasted about half an hour and which was followed by fever and sweat. After the chill he was drowsy and slept some. About a week after the beginning of the condition the patient had pain in the epigastrium and the pain had been located in that region ever since. For the four weeks preceding his admission the patient had an attack of chill, followed by fever and sweat, every day and sometimes he had two in a day. He never had more than two in one day. The patient had a good appetite but when he ate he felt as though his food was stuck in his eipgastrium before it entered the stomach. The epigastrium pain was constant.

Physical examination: Examination of the lungs showed no pathological signs except a slightly hyperresonant note at the right apex. Heart showed a rather weak and indistinct first sound with no murmurs. The second aortic sound was not accentuated. Abdomen was distended and tympanitic, and marked tenderness was obtained over the region of the gall bladder. There was no tenderness over McBerney's point. Liver dullness was increased downward and to the left. The lower margin of the organ was distinctly palpable two fingers breadth below the costal margin. The upper border of liver dullness extended to the fifth interspace. There was tenderness on pressure in the epigastric triangle and along the right costal margin as far as the anterior extremity of the seventh rib. The spleen was not enlarged. The patient was jaundiced. His mucous membranes were pale, his skin dry. His pupils were equal, reacted normally to light and accommodation. His breath was foul and his tongue was heavily coated with a brownish fur.

Examination of the blood gave the following results:

Erythrocytes	4,130,000
Leukocytes	42,320
Ratio	1—97
Hemoglobin (Fleischl), per cent	57
Color Index	0.69

Differential count.

Polymorphonuclear neutrophiles	92.2 per cent
Lymphocytes	1.4 per cent
Large Mononuclears	3.8 per cent
Transitionals	1.0 per cent
Myelocytes	1.6 per cent
	100.0 per cent

No malarial parasites found.

Examination of the urine gave the following results: Color, straw; reaction, acid; specific gravity, 1,030; a small amount of white flocculent sediment composed of leukocytes, amorphous urates and uric acid. No albumin, no casts.

Examination of gastric contents: The gastric contents were withdrawn after the administration of an Ewald test meal. Amount obtained, 60 c.c.; reaction, acid; odor, musty; fluid, milky white containing a small quantity of mucus, epithelial cells, leukocytes, starch granules, fat globules and fungi. Total acidity, 75, free hydrochloric acid present but the amount not determined; no lactic acid. The patient was advised to have an operation for the relief of his gall bladder condition, but the operation was refused and the patient was discharged at his own request.

This case is interesting because the patient was a man who had lived in a malarial district and who had malaria previously. In addition to that he was living in a district in which malaria is supposed to be prevalent. The physician who referred the patient to the hospital said that he had malaria, basing his diagnosis upon the frequent recurrence of chill, fever and sweat. The blood examination was made as soon as the patient was put to bed and a physical examination was made. The fact that there was a leukocytosis of 42,000 was a polymorphonuclear percentage of 92.2 disposed at once of the diagnosis of malaria. The absence of malarial parasites was, of course, to be expected in such a condition. Although no operation was done so that the diagnosis of empyema of the gall bladder could be confirmed, there is hardly any question but that that condition was present. The same history and results would be obtained in a case of amebic abscess of the liver which is usually treated with quinine under the impression that it is a case of malarial infection before its real nature is discovered.

CASE 15. DEFINITE DIAGNOSIS NOT MADE.

Male, white, native of Italy, aged two years, nine months; was admitted to the hospital (17740) in the service of Dr. Samuel McC. Hamill with a diagnosis of paralysis of the throat and hysteria. The mother said that the child would not eat because it was unable to swallow. These symptoms were of ten or twelve days duration.

Family history: Negative.

Previous history: The child was born at term after a normal labor. He was breast fed for sixteen months. He had had measles six months before his admission. He had never had diphtheria. Ever since the attack of measles the child had complained of throat trouble.

Present trouble: Ten or twelve days before admission the mother noticed that the child refused to eat. She said that it was often necessary to stop up the child's nose so that it could swallow. If this was not done, the food would sometimes regurgitate through the nose.

Physical examination (made by Dr. Hamill): The patient was very much emaciated; the skin was dry and very much relaxed; the superficial veins were prominent in the temporal region, on the abdomen and on the thorax; the parietal eminences were prominent; the vault of the cranium was flat; the head was square, and the fontannelles were closed. The teeth were decayed. There was a small infected wound in the upper portion of the right ear, but no other skin abrasion. There was some edema of the feet and legs. The abdomen was distended. The spleen was palpable below the costal margin. Abdominal resistance was marked on the right side. The liver could not be palpated. There was a transmitted tympanitic note over the entire chest; breath sounds were clear. The heart's action was regular, rapid and clear. The anterior cervical lymphnodes were about the size of a bean; the posterior cervical lymphnodes were about the size of a pea; the axillary lymphnodes were about the size of a large pea; the inguinal lymphnodes were about the size of a small pea. No masses were felt in the abdomen. A few scars were visible on the right arm and on the face which looked like the scars resulting from a local infection. There was no anal fissure and no evidence of muscular paralysis. The urine examination gave the following results: Color, light amber; reaction, acid; specific gravity 1.011; silght amount of granular sediment composed of urates. There was no albumin and no glucose.

Blood examination:

Erythrocytes	4,250,000
Leukocytes	8,700
Ratio	1—488
Hemoglobin, per cent	50
Color Index	0.68

Differential count:

Polymorphonuclear neutrophiles	40.6 per cent
Lymphocytes	41.4 per cent
Large Mononuclears	12.8 per cent
Transitionals	1.2 per cent
Eosinophiles	2.6 per cent
Myelocytes	1.4 per cent
	100.0 per cent

No malarial parasites were found.

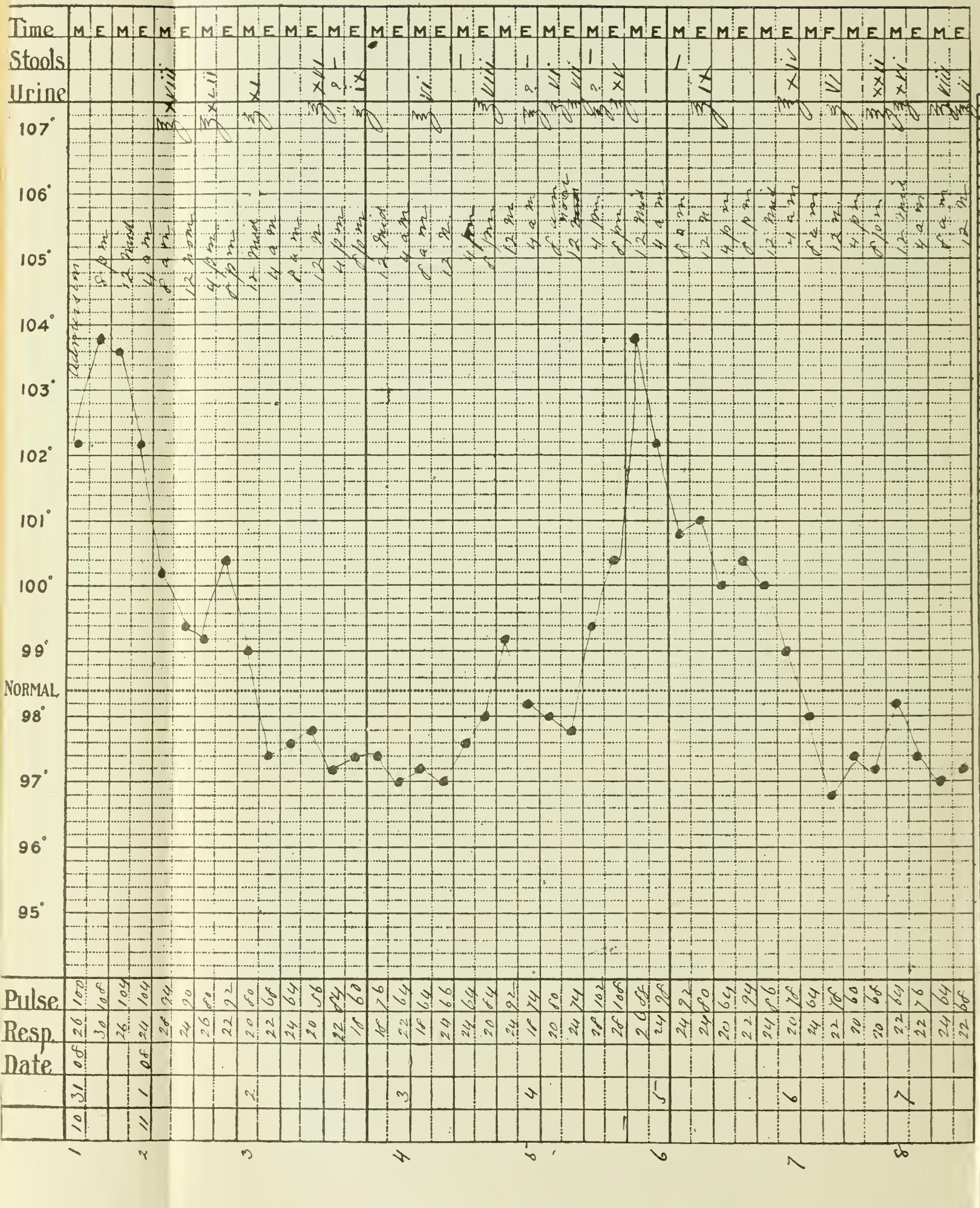
The second urine examination gave the following results: Color, amber; reaction, alkaline; specific gravity, 1,006; there was very little sediment, but the microscope showed numerous crystals of ammoniomagnesian phosphate. There was no albumin and no glucose

The second blood examination gave the following results:

Erythrocytes	4,520,000
Leukocytes	10,700
Ratio	1—413
Hemoglobin, per cent	80
Color Index	0.88

Differential count:

Polymorphonuclear neutrophiles	35.4 per cent
Lymphocytes	41.8 per cent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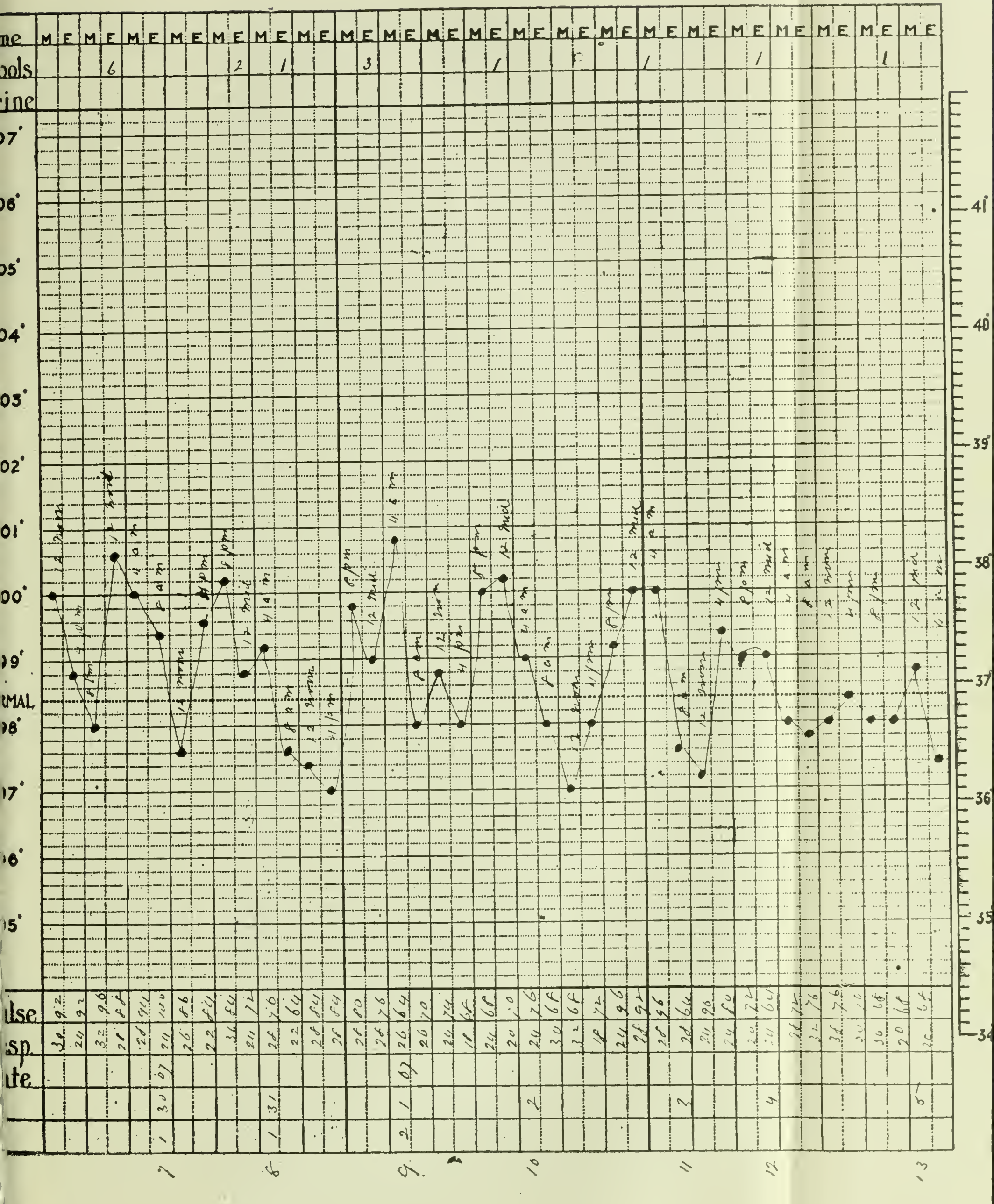
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Large Mononuclears	17.4 per cent
Transitionals	1.8 per cent
Eosinophiles	1.0 per cent
Basophiles	2.4 per cent
Myelocytes	0.2 per cent
	100.0 per cent

No malarial parasites were found.

During the patient's stay in the hospital a bacteriological examination was made of the secretion in the throat and diphtheria bacilli were found. The child's condition greatly improved, he became better nourished and, although his muscles were flabby, the knee jerks were present on both sides. There was no Babinski; the plantar reflex was more marked on the left than on the right. An examination of the eyes made by Dr. William M. Sweet showed that the pupils were clear and that they reacted normally. The occular rotations were good; the media were clear, and the fundus was normal in each eye. The patient had several attacks of crying which usually came on during the night or late in the afternoon. He had a discharge from the right ear for two days, and an examination, made by Dr. Walter Roberts, showed a double perforation of the right membrane tympani, which had been present for some time. The patient was finally discharged cured.

This is an interesting case in which a definite diagnosis was not made. The condition was one that some consultants who saw the patient with Dr. Hamill, in whose service the patient was treated, thought might be due to syphilis, but no definite conclusion concerning that point was made. The patient had a curious inability to swallow without previous diphtheritic history. During his hospital stay, however, a bacteriological examination of the secretion from the throat showed organisms resembling diphtheria bacilli. It is possible that this was a case of post-diphtheritic paralysis following a case of bacteriological diphtheria. On account of the nativity of the child, he was born in Italy, the question of malarial infection came up. There was no history of malaria obtained, but the large mononuclear leukocytes were increased on both occasions on which a differential count was made, 12.8 per cent at the first count, 17.4 per cent at the second count. No malarial parasites were found. The high lymphocyte percentage is, of course, accounted for by the age of the patient, two years and nine months. I think it doubtful if malaria had any relation of an etiologic nature with this case.

CASE 16. DEFINITE DIAGNOSIS NOT MADE.

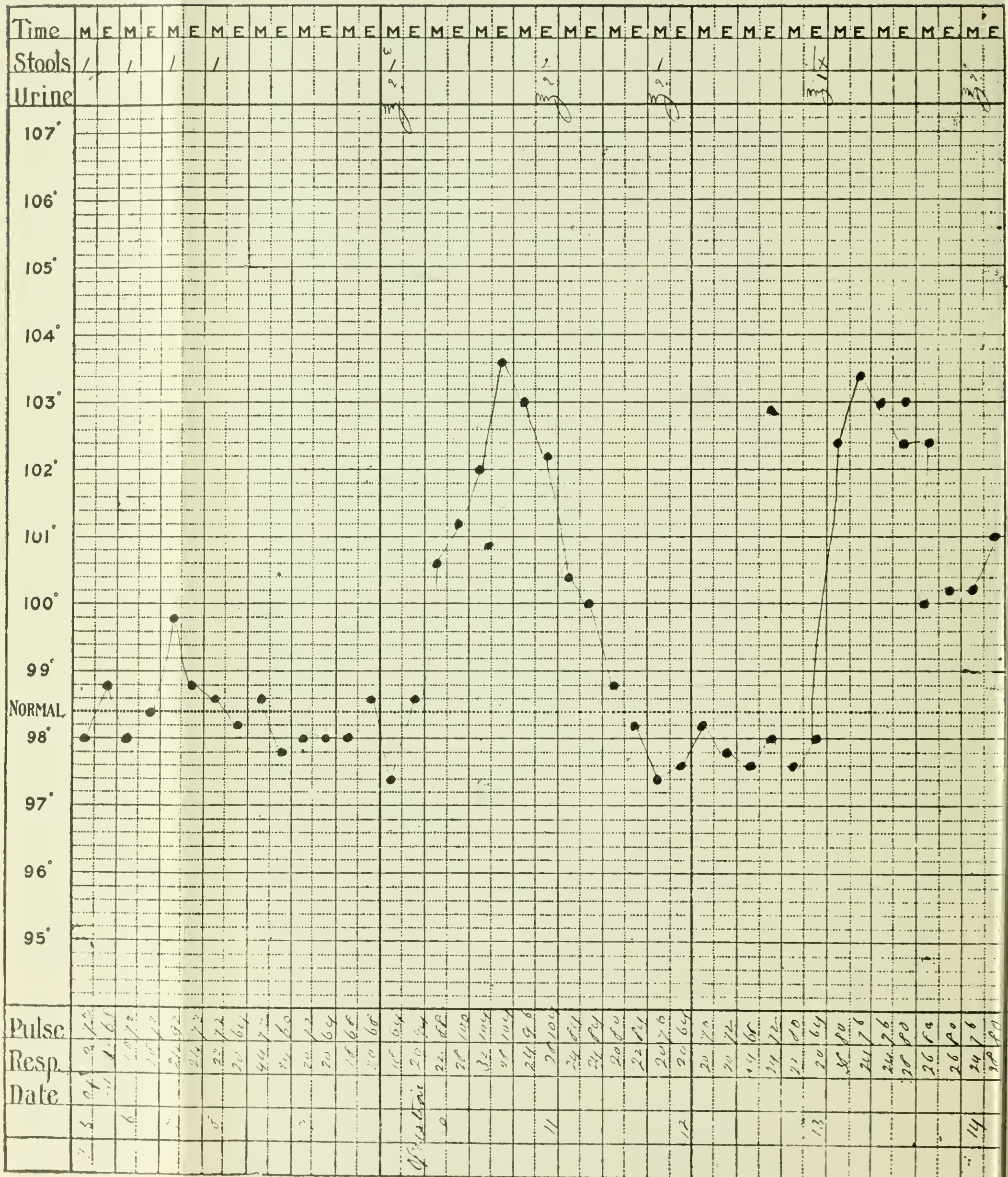
Male, white, a native of Russia; was admitted to the hospital (16316) in the service of Dr. A. A. Eshner, with a diagnosis of malaria.

Family history: Negative.

Previous history: Negative.

Present trouble: Five weeks ago the patient began to have chills. These came on as a rule every second day and sometimes every third day. They were so severe as to shake the bed and were followed by sweat, high fever and severe headache. The last chill before admission had occurred a week previously, but the patient had had a continuous fever since that attack. His bowels had been regular; he said that his urine had contained blood, and two weeks before admission he had developed a severe pain in the hepatic region which lasted three days.

On physical examination the patient was found to be a well nourished, white, male adult, about sixty years of age. The pupils were clear and reacted to light and distance. The tongue was slightly coated and moist. The cervical lymphnodes were enlarged on the right side but not on the left. There was a visible pulsation in the vessels of the neck. The chest was fairly well developed; the lungs were normal; the heart was normal except for a slight accentuation of the pulmonary diastolic sound; the abdomen was negative; neither the liver nor the spleen was enlarged. During his stay in the hospital the patient perspired a great deal. Examination of his urine gave the following results: Color, amber; reaction, acid; specific gravity, 1.029; a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very slight amount of sediment composed of epithelial cells and amorphous urates. There was no albumin and no glucose. The diazo reaction was positive.

Examination of the blood gave the following results:

Polymorphonuclear neutrophiles	58.6 per cent
Lymphocytes	5.4 per cent
Large mononuclears	29.6 per cent
Transitionals	2.4 per cent
Eosinophiles	2.6 per cent
Basophiles	1.4 per cent
	100.0 per cent

No malarial parasites were found. No pigmented leukocytes found. An agglutination test was made with bacillus typhosus in a 1 to 40 dilution, but was negative. An examination of the feces showed no ova, embryos, adult parasites, nor protozoa.

A second blood examination gave the following result:

Erythrocytes	4,540,000
Leukocytes	12,000
Hemoglobin (Dare), per cent	78
Ratio	1—378x
Color Index	0.85x

Differential count.

Polymorphonuclear neutrophiles	55.0 per cent
Lymphocytes	25.0 per cent
Large Mononuclears	12.5 per cent
Eosinophiles	7.5 per cent
	100.0 per cent

Erythrocytes	4,020,000
Leukocytes	11,000
Ratio	1—365x
Hemoglobin (Dare), per cent	70
Color Index	0.87x

Differential count:

Polymorphonuclear neutrophiles	58.6 per cent
Lymphocytes	5.4 per cent
Large Mononuclears	29.6 per cent
Transitionals	2.4 per cent

CONCLUSIONS.

My object in preparing and presenting this paper is to point out the conditions that are likely to be met with wherever that disease is present, which may seem on superficial examination to be due to malaria. If in a temperate climate one can meet with such diversified conditions that lead to the suspicion of the existence of malarial infection, surely in a subtropical or tropical climate, where cases of acute malaria and its sequellae are present in large numbers, problems such as those discussed in this communication will be more numerous and more difficult of solution. The point to be emphasized is that even when a clinical condition appears to be dependent upon malarial infection a careful physical examination, accompanied by a study of the condition of the blood particularly, and of the excretions and secretions in addition, will adduce important evidence to show the real nature of the case. I wish also to call attention to a method of estimating the degree of infection with malaria which appears in the detailed reports of the cases of malarial infection in the early part of the paper. By counting the number of parasites seen while one is enumerating a certain number of leukocytes, one can by making a proportion make an approximate estimation of the number of parasites in the peripheral blood of the patient. In case one there would be 1,152 parasites to the cubic millimeter of blood; in case two there would be 73,100 to the cubic millimeter; in case three, 16,992; in case five, 1,480 to the cubic millimeter.

My thanks are due to Dr. A. A. Eshner, Dr. David Riesman, Dr. R. Max Goepp, Dr. Samuel McC. Hamill, Dr. William M. Sweet, Dr. James H. McKee, and Dr. B. F. Baer for the privilege of using the clinical material made in their wards in the preparation of this paper.

A Case of Pellagra Caused by Amylophagy Resulting From Uncinariasis. -:- -:-

BY

C. C. BASS, M. D.

New Orleans

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A CASE OF PELLAGRA CAUSED BY AMYLOPHAGY RESULTING FROM UNCINARIASIS.

BY C. C. BASS, M.D., NEW ORLEANS.

Mrs. C., aged 23, white, from McComb City, Miss., referred by Dr. Webb, for probable pellagra. Her history is negative for any of the early symptoms of pellagra, until March, 1909, when she had sore mouth and bowel trouble. She had this again in November, and was in poor health all summer, but no skin symptoms occurred that the patient recognized. Leucorrhea, female troubles and melancholia were among her symptoms and she was taking medicine most of the time. She was also troubled with "indigestion" often.

During the winter the patient's health improved. About six weeks ago, the middle of April, her previous general poor health returned and there occurred an erythema on the backs of her hands. This was followed by exfoliation and now, June 1st, presents the typical and unmistakable appearance of pellagra. There is no other distinct skin lesion, but the skin of the face over the malar, prominences of the forehead and the chin is distinctly rougher then elsewhere. She has had during this time diarrhœa, "indigestion," epigastric burning, sore mouth, melancholia, nervous spells and has rapidly weakened. Her baby, ten months old, who was breast-fed only, had bowel trouble, thought to be due to teething, at the same time the mother developed diarrhœa this time, but has since gotten well, though she has continued to nurse it.

The patient's tongue is red-edged, and studded on the edges and tip with large raised red papillæ. The mucous membrane of the mouth is very red, but no ulcers present. The patient says she has had an extra flow of saliva the past three weeks. She has the blank melancholic expression frequently seen in the terminal stages of pellagra, and also the corresponding mental hebetude. Knee jerks are absent and there is no reasonable doubt that the case is one of pellagra in the terminal stage. This diagnosis was concurred in by Dr. Menage, who also kindly examined the patient for me.

The patient and her husband say that she eats less corn bread than either he or their two children, all of whom are well. Corn bread is, however, eaten one or more time a day. Further inquiry reveals the fact that in the winter of 1906-7 the patient took up a peculiar habit of eating raw starch. The habit grew on her until in a few months she was eating a pound, and sometimes more, a day, largely to the exclusion of other food. This she continued until six months ago, when her husband forced her to quit it, so he thinks, and she claims. The patient admits that she still craves it and the history is that she was secretive about the habit when she was eating large quantities. The starch eaten was the common laundry starch sold in bulk in the stores. The particular brand will not be stated here for apparent reasons. On further examination the patient was found to have a moderately severe hookworm infection, a well known source of perverted appetites. Further evidence that this was the cause is the history, that during the summer prior to the beginning of this peculiar habit of starch-eating or amylophagy, she had an attack of ground itch, which probably indicates the time the hookworm infection occurred. She also had it in 1907 and 1908.

The following conclusions seem fully justified by the history and examination:

I. The patient has pellagra.

II. The patient has been an exclusive starch-eater a few months or a year before recognizable symptoms of pellagra developed, and has continued the habit.

III. The history of ground itch indicates that the hookworm infection antedated the amylophagy.

IV. Inasmuch as hookworm disease is a frequent source of perversions of appetite, it is reasonable to presume that we have in this instance a case of pellagra indirectly caused by hookworm infection.

V. The cause is further evidence of the correctness of the maize theory as to the cause of pellagra and a warning against the use of foods made from corn of doubtful quality, such as corn starch, corn syrup, corn whiskey, corn flakes, etc.

741 Carondelet Street.

A CASE OF STRONGYLOIDES INTESTINALIS WITH LARVÆ IN THE SPUTUM *

JOHN G. GAGE, M.D.
NEW ORLEANS

Although infection with *Strongyloides intestinalis* is by no means uncommon in the South, patients with larvæ in the stools being frequently observed by physicians, nevertheless the number of reported cases is not large and is not a true index of the prevalence of the disease. This is probably due to the fact that this parasite is usually considered harmless.

In the case here reported the larvæ were discovered first in the sputum. The patient entered the hospital with a diagnosis of pneumonia. His temperature promptly dropped to normal but, because his general condition did not improve and because of impaired resonance and later expectoration, tuberculosis was suspected and his sputum examined.

I saw the first larvæ while examining the fresh sputum; and thought they might be a contamination of some sort, because the patient had vomited that day and the sputum contained food particles and milk; but, on the following day, Dr. Dock found them in a fresh bit of sputum just coughed up by the patient. Fresh sputum was examined almost daily during the patient's stay in the hospital and on careful search larvæ could always be found, so the idea that the larvæ came from elsewhere than the respiratory tract was abandoned.

They were slender worms, measuring 0.43 mm. to 0.45 mm. in length by 0.02 mm. in breadth, and having a long cylindrical esophagus which occupied nearly all the anterior half of the worm. The idea that they were hookworm larvæ was ruled out at once, and, after a short search through the books, it was decided they were some variety of strongyloid, and as such they were reported by Dr. Dock before the Orleans Parish Medical Society. Later, after they had been studied in connection with the larvæ obtained by incubating the stools, they were identified as the filariform larvæ of *Strongyloides intestinalis*. The larvæ in the sputum did not have the characteristic serpentine motion of filariform larvæ, their movements consisting of coiling and uncoiling. This was probably due to the tenacity of the sputum and the pressure of the cover-glass. I saw one or two larvæ in which the sexual anlage was present, which would point to their being but a few hours old.

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*From the Medical Clinic of Dr. George Dock, and the Charity Hospital, New Orleans.

Examination of the stools showed enormous numbers of larvæ, identified as the rhabditiform larvæ of the *Strongyloides intestinalis.*

Nematodes and their larvæ are described as occurring in various parts of the body of man and animals. Braun[1] speaks of instances in which they have been found in the skin, heart, blood, eye, urethra, subcutaneous tumors, and bronchial lymph-glands. Richard,[2] in discussing Siler's paper on uncinariasis, mentions a patient with chronic bronchitis whose sputum contained hookworm larvæ.

REPORT OF CASES

History.—The patient, H. G., white man, age 48, a painter by occupation, entered Charity Hospital Oct. 16, 1909, complaining of chills and fever. Family history was negative. The patient was born in New Orleans and lived here until about 16 years of age, when he went to work on board a ship. He said he "followed the seas for four years and was all around the world"; came back to New Orleans and had not been out of the city since. He used tobacco and was a heavy drinker. He had worked at his trade as a painter for twenty years. He said that he had always eaten all the green vegetables he cared for and drank "all kinds of water and whenever I can get it." He had had the usual diseases of childhood; had malaria when young. He never had scarlet fever, typhoid fever or diphtheria. He denied venereal disease; had always been healthy. He said that he had not lost a day's work because of illness in thirty years. He had been feeling ill for a week or ten days and, two or three days before coming to the hospital was taken with a chill while on his way to work and felt so miserable that he went home. A physician was called who told him he had "typhoid-pneumonia" and advised him to enter the hospital. He entered at the crisis of a lobar pneumonia involving both upper lobes.

The signs rapidly cleared and, November 22, there was merely slight dulness above, with dull tympany below, feeble breath sounds, piping râles, and, on cough, abundant moist râles. At the right base crackling persisted. The patient was emaciated, with harsh, dry skin and muddy complexion.

Laboratory Findings.—Sputum: About 5 c.c.; pale yellow; mucopurulent; tenacious; blood-streaked in places; slightly fetid odor. No tubercle bacilli; many large cocci and short thick rods. No elastic tissue. One imperfect spiral. Many food particles and much detritus from mouth. Fifteen or twenty larvæ were seen.

Blood: Red cells 3,020,000. White cells 13,300. Hemoglobin 70 per cent. (Tallqvist). Differential count, 500 cells counted: Small lymphocytes 13.2 per cent.; large lymphocytes 2.0 per cent.; transitionals 1.4 per cent.; polymorphonuclears 79.8 per cent.; eosinophils 3.2 per cent.; mast cells 0.4 per cent. Few microcytes, no macrocytes, few poikilocytes. No nucleated red cells.

Urine: Turbidity marked. Specific gravity 1013. Reaction alkaline. Color pale yellow. With heat and nitric acid, very small precipitate. With acetic and potassium ferrocyanid, slight precipitate. Fehling's test no reduction. Foam white. Sediment large. Large amount of pus. No larvæ.

Stool: Small light brown, semisolid. Odor fecal. Enormous numbers of larvæ. No flagellates, no amebas. One trichocephalus egg. One Charcot crystal.

Course of Disease.—Three times during the patient's stay in the hospital I found eggs in the fresh stool. On two occasions the egg contained dead embryos, once well preserved, the other time brown, granular and badly disintegrated.

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1. Braun: Animal Parasites of Man, 1899.
2. Richard: Post-Grad., 1909, xxiv, 475.

None of the eggs seen in the stools was in segmentation nor were they likely to have been mistaken for hookworm eggs.

Because of the weakened condition of the patient, and in view of the fact that nearly every one agrees that it is useless to try to get rid of the worms in the intestine, our patient received no anthelmintic.

When he entered the hospital he had fever of 101-105 F., which lasted about two days, after which time he was afebrile during his stay, with the exception of two slight flurries, each lasting about a day, the temperature rising to 101 on one occasion and to 100 on the other.

At first the patient had no cough and no sputum, but later a slight cough developed with scarcely any sputum, so that it was difficult to get any for examination, but finally a specimen was obtained in which larvæ were found. At first the sputum had somewhat the appearance of material from bronchiectatic cavities, but had not the foul odor. Later the sputum became more abundant and bronchitic in character. While the sputum was scanty the larvæ were fairly abundant, several could be found in looking over a few low-power fields, but as the sputum became more copious a longer search was required; sometimes one had to look over as much as 5 c.c. before one larva could be found. But one could always find them after a long enough search.

As Teissier has reported filariform larvæ in the circulating blood, large amounts of this patient's blood were examined, but no larvæ were found.

The patient's appetite was very poor and he ate scarcely anything, but previous to this illness he had always been a hearty eater. After he had been in the hospital about three weeks he had attacks of vomiting for three or four days, apparently without much nausea. After this time he would take no nourishment except a small amount of tea or soup and a few crackers.

After he had been in the hospital about one week he developed a diarrhea, passing from ten to twelve stools in the twenty-four hours. The diarrhea was most marked in the early morning hours, when he would pass seven or eight stools between 4 and 6 a. m. This lasted but a few days and then for a week or ten days he was free from diarrhea, with but one or two soft stools per day. During the rest of his stay in the hospital, periods of diarrhea occurred about every two weeks. The stools were always soft and when the patient had diarrhea they were thin but never dysenteric in character.

He had one other symptom which is common in infection with *Strongyloides intestinalis*, namely, the desire to go to stool was very urgent, and he had to defecate at once, even when the stool was of normal consistency. He said that he had never been troubled with diarrhea, but after drinking bouts his stools were more numerous and thinner than usual. This never lasted longer than one day. He had noticed this for the last four years.

The patient was personally very filthy, and the sheets were always wet and smeared with feces. The skin over his back and buttocks was red and irritated, and a bed-sore developed over the sacrum.

The patient grew weaker, his cough worse and sputum more abundant and, although during the last few days he complained of some shortness of breath, he had no fever and examination of his chest showed nothing other than signs of a diffuse bronchitis.

He died Dec. 17, 1909, after having been in the hospital two months.

The histological findings in this case are recorded in a paper read before the meeting of the American Pathologists and Bacteriologists at Washington.† Briefly, the findings were as follows:

Macroscopic Post-Mortem Examination.—There was catarrhal inflammation and superficial ulceration of the small intestines. Mucus from the duodenum contained large numbers of adult worms, active rhabditiform larvæ and eggs in all stages of development. The eggs, while numerous, were few in proportion to the number of larvæ. There were many larvæ, a few eggs, but no adult worms in the mucus from about the middle of the ileum. There were numerous areas of fresh bronchopneumonia throughout the lower lobes of both lungs. Sputum taken from the trachea and bronchi contained a few larvæ. The pelves of both kidneys were distended with pus. The other organs were apparently negative.

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†Gage: Jour. Med. Research, 1910, xxiii, 177.

Microscopic Post-Mortem Examination.—Sections of the small intestine showed adult worms, eggs and larvæ in the lumen of the intestine and in Lieberkühn's glands, as has been described by many others. In addition to this I found larvæ in lymph-spaces and lymph-vessels, in the muscularis mucosæ, submucosa, between the muscle coats and beneath the serosa. I could find none in blood-vessels. In the sections of lung I found one larva in an antevesicular tube, another in the perivascular tissue between two lobules, and a third in an air-vesicle.

In addition to the above case I have seen larvæ in stools from fourteen other persons: four students (two from Louisiana, one from Mississippi, and one from Tennessee); one patient in Charity Hospital who has always been a resident of Louisiana; three other patients in Charity Hospital and two in Touro Infirmary who left the hospitals before I had an opportunity to get histories from them; three children under the care of Dr. Irwin, who kindly sent me specimens of their stools, and one other person whose stool was sent by a medical student to the Clinical Laboratory for examination. The following case report was sent to me by Dr. Allan C. Eustis and is included by his permission:

Case 2.—Patient, Mrs. G., white woman, aged 41, wife of a farmer and mother of six children, was a resident of Lafourche Parish until six years ago, when she moved to Vermilion Parish. Family history is negative. She had been in good health all her life and never complained until July, 1907, when she began having headaches, edema of the face and ankles, weakness and pains in the limbs and gradual emaciation. I first saw her on Oct. 11, 1907, in consultation with Dr. Cushman.

Examination.—This showed a flabby condition of the muscles, sunken eyes and considerable weakness. There was no tenderness of any of the abdominal viscera and the heart and lungs were negative. Liver and splenic dulness were not noticeably increased. The abdominal wall was very much relaxed. There was no history of diarrhea and the stools were normal in appearance. Pulse was 120 and of low tension; respiration 18 per minute. Temperature was normal and had been so from the beginning of the attack. No plasmodia. Hemoglobin 80 per cent. Tallqvist. Leukocytes 11,500. Red blood cells 4,625,000. The patellar reflexes were entirely absent, but there was no Romberg's symptom or Argyll Robertson pupil. Closer examination of the muscles of the lower limb showed the peroneal group of muscles absolutely non-reactive to the faradic or galvanic current.

The differential blood-count at this time showed 56 per cent. eosinophils and this led to an examination of the stools, which at first were negative but, after administration of a full dose of Epsom salts, showed myriads of rhabditiform embryos of *Strongyloides intestinalis.* They were at first mistaken by me for trichinæ and a proper anthelmintic was sought. Thymol and the others having no clinical effect, the embryos were subjected to various solutions while under the microscope. Among these were thymol, santonin, male-fern, calomel, quinin bisulphate, glycerin, liquor formaldehydi and salicylic acid. Only two had any effect. Liquor formaldehydi was found to kill the embryos, but had to be used in such strong solution that the intestinal canal would not tolerate it. Phenyl salicylate (salol) was then tried with excellent results.

Treatment and Course of Disease.—The patient was put on three-grain doses of salol every three or four hours and kept on the following soluble diet for one month and a half; chicken, beef and oyster bouillon, gelatin, fruit-juices, sugar-candy and a dozen raw eggs per day. The patient never lost weight. In addition she was given enemas of a gallon of salt solution containing one of the mild antiseptics. The number of embryos began to diminish from the time we placed the patient on phenyl salicylate and they finally disappeared. The muscles were treated by daily applications of the faradic current with complete recovery. Today the patient is absolutely well and, while I have made examinations of her stools, even after the administration of a saline, I have not been able to find the eggs or embryos since she was discharged. The eosinophils have diminished also, showing only 2 per cent. at the last count made, about a month ago. Jan. 17, 1910, patient is still in perfect health and careful examination of the stools fails to reveal the presence of any embryos.

RESULTS OF CULTURES

I attempted to grow the larvæ found in the stools and to repeat the work of others along this line. Stools containing larvæ were placed in an incubator at 37 C., on top of the incubator at about 30 C., and at room temperature; but a temperature of 30 C. was most suitable. Portions of the stool were put in moist sterile sand and on moist filter-paper, but the larvæ grew quite as well in the stools themselves. I soon found that the larvæ grew best when the stool was the consistency of a thick paste; that when it was too firm or too fluid they did not do so well; also that the amount of air present had to be considered, for, if the stools were placed in closed containers, most of the larvæ died, either from lack of oxygen or because of the high gas pressure developed by fermentation. The work with the larvæ from the first case was carried on by incubating the stools themselves in open dishes at 30 C.

As it was not possible to follow accurately the development of any given larva when growing the larvæ in the stools, I adopted the following technic, after many modifications: By means of a capillary pipette the larvæ were picked out of smear preparations and placed in distilled water in a watch-glass, and, after a second washing, were put on the medium and incubated at 32 C. in a moist atmosphere. In this way I got rid of the fecal matter and the greater part of the bacteria and could plant as many larvæ as desired. This method is especially desirable when stools contain few larvæ.

This prevents contamination with other nematodes and avoids the criticism brought forward by Leiper[3] concerning Ozzard's observations on *Ankylostoma duodenale.* Leiper rejected Ozzard's results because sufficient precautions against contamination had not been taken. He suggests that the cultures may have been contaminated by the water or sand used, or that the source of contamination had passed through the alimentary canal of the patient. He says:

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[3] Leiper: Brit. Med. Jour., November, 1909, p. 1332.

When we remember that free-living nematodes abound in all soil and vegetables, that their eggs and larvæ are able to withstand a considerable degree of drying and that they multiply exceedingly in the course of a few days, we should be very loth to accept results of experiments that do not rigorously exclude the possibility of their presence.

Watch-glasses are more convenient than Petri dishes, because the larvæ are kept within a smaller compass and because the sides of the Petri dishes prevent the examination of the edge of the medium. It is convenient to use a very low-power objective, which has the advantage of a large field and plenty of room between the objective and the stage. Slides 2 by 3 inches are much better than the usual 1 by 3 because more material can be examined and much time saved.

The following medium, a modification of the Hiss semisolid medium, was suggested by Dr. Duval, and was found most suitable, because in it the larvæ can move about freely and can be followed through all stages of development.

1000 c.c. distilled water.
80 gm. gelatin.
10 gm. agar.
5 gm. beef extract.
Boil, clear and titrate to 2 per cent acid.

When incubated at 32 C. the sexes can usually be distinguished in about twelve hours and are fully developed in twenty-four hours: however, it sometimes happens that twice that length of time is required. Development may be greatly retarded by a more thorough washing of the larvæ before planting them on the medium, or by incubating them at 25 C. instead of 32 C. I was not able to hasten their development by incubating them at 37 C. When a large number of larvæ are planted it is often noticed that they do not all develop uniformly, that some have already coupled and the females contain eggs well-advanced in segmentation before others have shed their skins. Often there are a few which develop much more slowly and, instead of maturing in twenty-four hours, require forty-eight or more, often dying before fully developed. Those which survive usually develop into filariform larvæ.

I noticed, in growing the larvæ from different cases, that the larvæ in some cases will nearly all develop into filariform larvæ, the proportion of sexual forms being about 1 to 100, and the sexual forms all males. In other cases the sexual forms predominate, the proportion of filariform larvæ being 1 to 25; and in these cases there are more females than males, the proportion being 1 to 6 or 8. This has been noted by others and is discussed in Thayer's article, but no satisfactory explanation has been offered. I believe that it is possible to determine into which of these groups a given case will fall, by careful examination of the larvæ in the stool. In those which develop into sexual forms the sexual anlage is more prominent; it appears larger, more hyaline and refractive, and is easily seen with a low power objective. In those which develop into filariform larvæ the sexual anlage appears somewhat smaller, less refractive, and more difficult to see, often a high-power objective being required to find it.

I have followed Thayer[4] very closely in describing the rhabditiform and filariform larvæ, because his description is excellent.

Rhabditiform Larvæ.—In the fresh stools these measure all the way from 0.225 to 0.45 mm. in length, by 0.02 to 0.03 mm. in breadth. The worm diminishes slightly in size toward the head and gradually tapers down to a sharp-pointed tail. The periphery is somewhat refractile, while within, the substance is filled with glistening, refractive, fat-like granules which are much larger toward the head than toward the tail. The mouth of the worm appears, as far as it can be made out, to consist of a simple funnel-shaped depression. The esophagus, between one-third and one-fourth the length of the worm, shows a long bulb-like enlargement at the head, followed by a constriction, which is succeeded by a second round or ovoid enlargement, in the middle of which is a triangular opening; the outlines of this opening are glistening and refractive, indicating clearly the tridentate, chitinous armature described by other observers. The outlines of the cells bordering the digestive tract, of which in some instances a slight suggestion can be made out, are as a rule entirely hidden by the glistening granules above mentioned. The anal outlet is situated at a distance equaling about one-tenth the length of the worm from the tip of the tail. The anterior lip of the anal outlet is slightly raised. A little below the middle of the worm, on the same side as the anal opening, is a small clear elliptical area, the rudiment of the sexual apparatus. The worms manifest a very active serpentine motion and, in many, repeated and violent muscular contractions of the esophagus are observed; these are especially marked about the tridentate opening, which appears to open and shut with considerable force.

Filariform Larvæ.—These are longer and more delicate in structure, measuring 0.4 to 0.55 mm. in length, and from 0.016 to 0.022 mm. in breadth. The distinct esophageal enlargements are lost and all trace of the rudiment of the sexual gland has disappeared. Though the parasite is more delicate as a whole than the younger embryo, the tail is blunter and more truncated. They are more active, showing most striking serpentine movements.

I have noticed that when larvæ from a case in which filariform larvæ predominate are planted, they collect at the edge of the medium in ten to twelve hours and one often sees writhing masses of from ten to thirty or more. Even in this short time the sexual anlage has disappeared, one is seldom seen, and never in a fully developed filariform larva. Braun's picture[1] of the filariform larvæ shows the sexual anlage, but there is no reference to it in the original article. The larvæ remain at the edge until they molt, which they do in from twenty to twenty-four hours, after which they are found all through the medium. Probably they collect at the extreme edge because the medium is firmer there and their skins are more easily shed. These larvæ are much more active than the sexual forms and are not often seen lying quiet until they are several days old. When placed in a drop of water under a cover-glass their movements are much more violent and in a short time the worms are to be found at the extreme edge. I have never been able to observe them feeding. They are more resistant, live longer, and grow under conditions which would be unfavorable to the development of the sexual forms. On only one occasion were they found in the fresh stool and then but three were seen.

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[4] Thayer: Jour. Exper. Med., 1901, vi, 75.

My own observations, except for a few points mentioned below, agree so completely with Strong's,[5] that I quote his description of the free-living adult males and females:

> *Free-Living Adult Females.*—"The females are longer than the males; their bodies also taper more in the posterior portion. They measure generally from 1 mm. to 1.4 mm. in length, and from 0.05 mm. to 0.075 mm. in breadth. In the adult free-living generation the esophagus has the same form as that of the larvæ, except that it shows a relatively smaller increase in length, measuring now about 0.16 mm. Of the three portions of the esophagus the buccalic is the longest. It measures 99 microns and represents in consequence a little more than half of the entire apparatus. The cephalic extremity is rounded and pierced by the mouth, about which, on careful examination, three or four papillæ can be made out. Next to the mouth comes a vestibule, which for a short length presents a gradual enlargement. It is much better developed than in the larvæ, and enters the anterior extremity of the esophagus, which juts from its interior in the form of a smooth cone. This part of the esophagus is continuous with the bulbous or terminal portion, which encloses an apparatus for trituration consisting of three chitinous teeth. .... The intestine of the female is somewhat longer than that of the male. It ends, as in the larvæ, in a papilla at the right side of the body at the base of the tail and often protrudes a little. In the females the posterior extremity of the body stretches itself out into a tapering, thin, fine tail, often lightly coiled into a spiral. A little below the middle of the body and on the right side is the vulval opening, marked by a slight contraction and giving access to a double uterus, the horns of which extend, the one anteriorly, the other posteriorly. Each of these ends in an ovary. The eggs measure 70 by 45 microns. They are elliptical; the shell is delicate and the vitellus contains a few granules. The eggs are often more or less segmented when laid. Indeed, not infrequently they hatch in the body of the adult, and one can then see the embryos moving within the body of the mother. As a rule, hatching is completed in twenty-four hours. At first the worms are thin, the tails are tapering, and the bulbous swelling of the esophagus and the chitinous teeth are apparent. They soon change and pass from the rhabditiform to the strongyloid stage."

In my observations I never saw the tail of the female coiled into a spiral, as described above. After coupling, eggs appear first at the vulva

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[5] Strong: Johns Hopkins Hosp. Rep., 1902, x, 91.

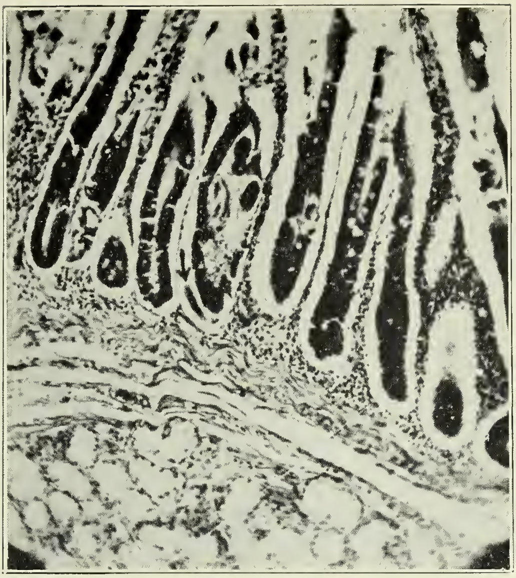

Fig. 1.—Larva at the bottom of one of Lieberkühn's glands just inside the basement membrane on its way to the close-meshed system of lymphatics in the mucous membrane. The arrows indicate the location of the larvæ. This and the following illustrations show sections of intestine and lung from Case 1.

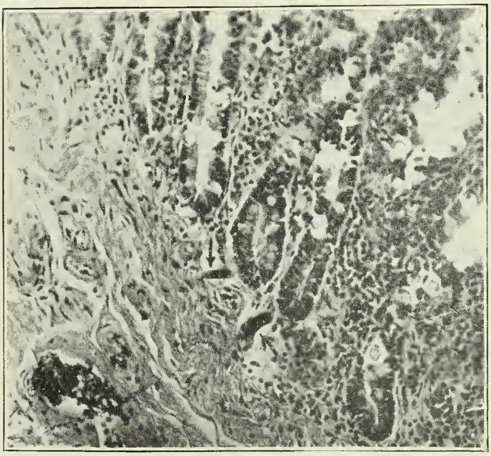

Fig. 2.—Larva breaking through into the muscularis mucosæ probably in a lymph-vessel.

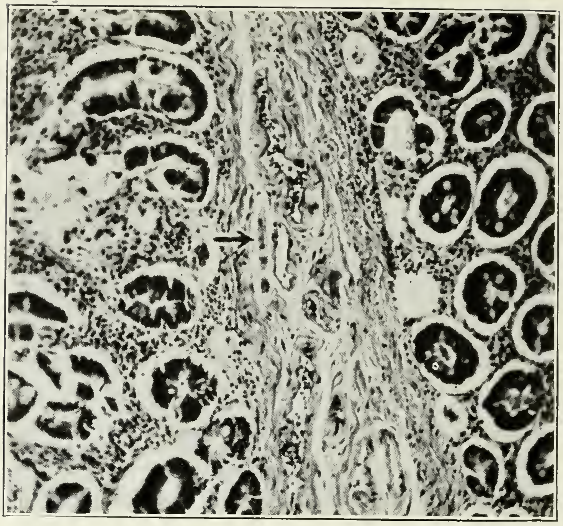

Fig. 3.—Larva in a lymph-vessel in the muscularis mucosæ of a valvula conniveus.

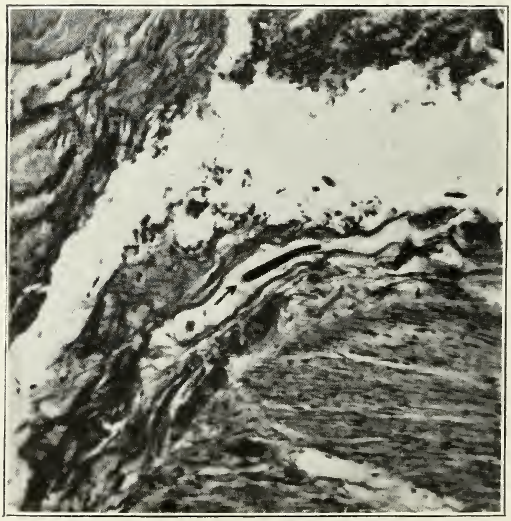

Fig. 4.—Larva in a large lymph-vessel deep in the submucosa, close to the inner circular muscular layer.

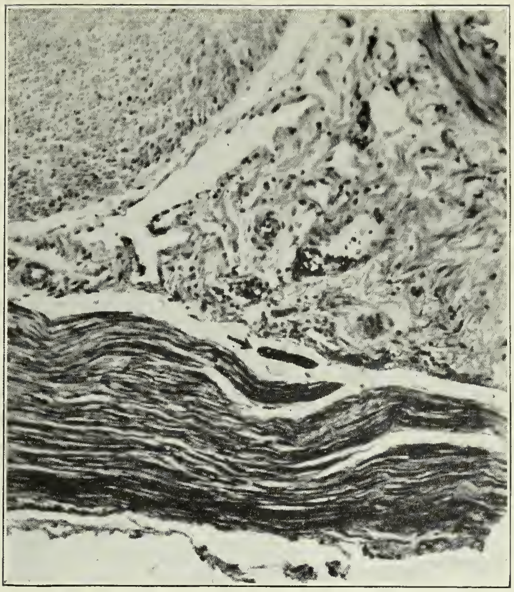

Fig. 5.—Larva just inside outer longitudinal muscular coat of the duodenum.

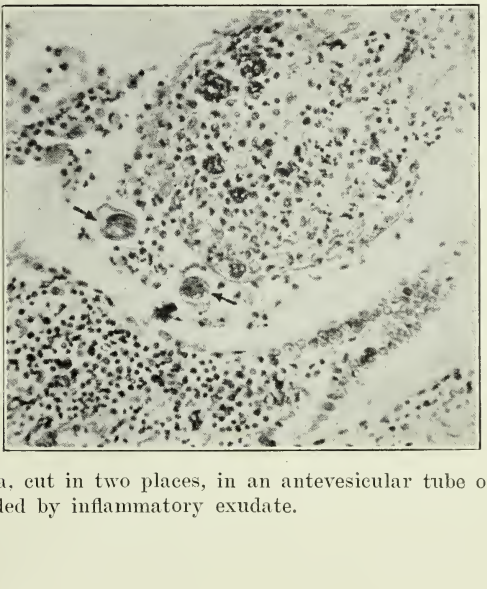

Fig. 6.—Larva, cut in two places, in an antevesicular tube of the lung. The larva is surrounded by inflammatory exudate.

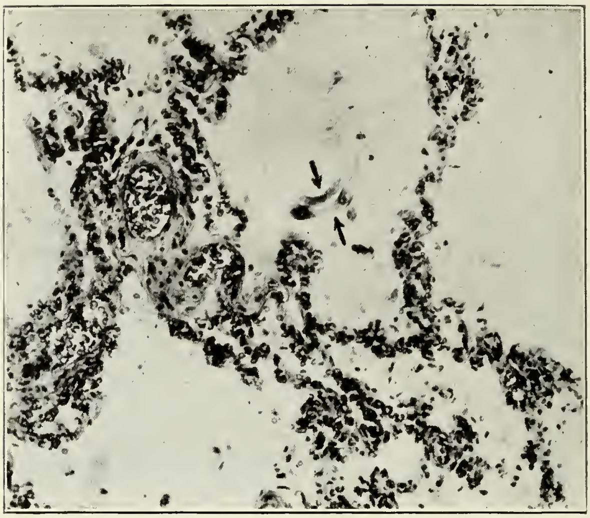

Fig. 7.—Larva coiled up in an air-vesicle. Portions of two coils shown.

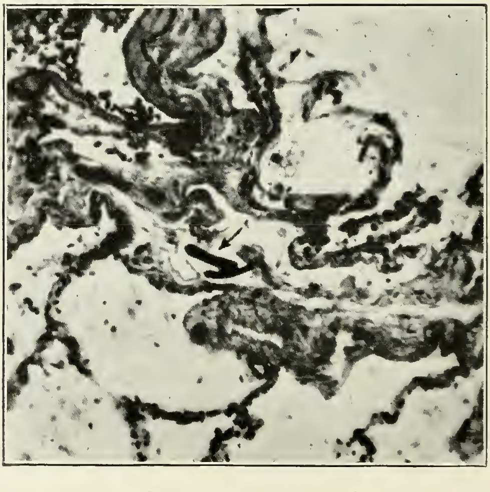

Fig. 8.—Larva in the interlobular connective tissue of the lungs.

and develop rapidly in both directions until there are sometimes as many as twenty-six, closely packed and lying transversely, which is quite different from the arrangement of the eggs in the body of the parasitic mother worm in the intestine. Those nearest the vulva are most developed and often contain embryos, and one can trace all stages of segmentation as either extremity is approached. The eggs when laid usually contain embryos. Unfertilized eggs segment to the mulberry-mass stage but no further. The females produce but one batch of eggs and I have never seen them couple the second time.

Free-Living Adult Males.—"The males are shorter and thinner than the females, measuring from about 0.75 to 1 mm. long by 0.04 to 0.06 mm. wide. The esophagus is a little shorter than in the female. The caudal extremity measures about 70 microns; it tapers quickly and is curved on itself in a manner quite different from the spiral coils in the tail of the female. Just at the base of the tail one can readily distinguish two cone-shaped and curved spicules, which represent the copulatory organ."

Cline describes a long gland made up of globules which is situated in the posterior third of the male and terminates at the base of the tail. I have often seen this; the globules appear to be small granular cells, larger and more granular at the posterior end. The gland extends through the middle third of the worm, but at this place is hard to see, and is sometimes indistinct. I have often seen the worm rupture at the base of the tail and the gland cells flow out. This is most often observed in old males. Between the posterior end of the gland and the spicules are two clear oval cavities. When placed under a cover-glass the males are sometimes seen to protrude and retract the spicules, one at a time. This occurs just before they die. On the tip of the tail is a delicate flagellum which is 30 to 40 microns long, 5 microns broad at the base and tapers to a fine point. This is easily seen when the worms are in the yellowish semisolid medium but, when placed in water, it is very easily overlooked. I have never seen this described, nor have I seen it represented in drawings.

Both sexes shed their skins and couple in from twenty to twenty-four hours. When about to couple the female lies quiet except for a movement of the head and a rapid rhythmic contraction of the second bulb of the esophagus. The male crawls around the female five or ten minutes before grasping her, stopping often and coiling his tail. He then coils the posterior half of the body around the female, so that the body of the male lies in a plane at right angles to the body of the female. Often two and sometimes three males are coiled around the female at the same time. After coiling his tail loosely around the female near the head the male begins to move around and around, feeling with the spicules while the female crawls slowly through the loop until the vulva is reached, when the coils tighten and the spicules are pressed in. The female does not struggle to get away as described by Perroncito,[6] who says, "She makes an effort as if to disengage herself." The worms remain in this position from three and one-half to five minutes; then the male uncoils and lies quiet for five to seven minutes and the female crawls away. Again my observations disagree with Perroncito who says, "The act has a short duration of from forty to fifty seconds." I have seen copulation many times and the time required for it was never less than three minutes. After a female has coupled she is not again approached.

In twenty-four hours after coupling the young larvæ are found free in the medium. These have an esophagus with a double dilatation, an oval sexual anlage—in fact, the same structure as in the larvæ found in the stools. This generation always died, so I was unable to watch its further development.

The larvæ feed on the bacteria or their products and not on the medium. When transferred to fresh medium they remain among the bacteria transferred with them and move away from the point of inoculation as the bacterial growth spreads. While feeding, the worms lie quiet, except the anterior end, which is in constant motion. The second dilatation of the esophagus shows strong rhythmic contractions which extend forward to the mouth and the entire esophagus moves up and down within the worm with each contraction. When the bacterial growth becomes too profuse, the worms die, if not transferred to fresh medium. By transferring them every day or every second day I have been able to keep the females alive four to six days after reaching maturity, but the males lived only half as long.

PREVALENCE AND DISTRIBUTION

Baetjer,[7] in a recent article, expresses the opinion that strongyloides infection is apparently quite uncommon in this country; but I agree with Stiles, who believes that it is common, especially in the Southern States. Baetjer found but fourteen cases reported in the United States which, with his case and six others in the Johns Hopkins hospital statistics, made a total of twenty-one. I find twenty-nine cases mentioned which, with Baetjer's seven, Eustis' one and my fifteen, make a total of fifty at the present time: Strong,[5] one case; Thayer,[4] two additional ones; Ohlmacher,[8] one; Price,[9] one; Moore,[10] one; Brown,[11] three; Hall,[12] one;

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[6] Perroncito: Quoted by Strong.

[7] Baetjer: Bull. Johns Hopkins Hosp., 1910, xxi, 118.

[8] Ohlmacher: Am. Med., 1903, v, 816.

[9] Price, Marshall Langton: Occurrence of the *Strongyloides Intestinalis* in the United States, Jour. Am. Med. Assn., 1903, xli, 651.

[10] Moore: Am. Med., 1903, v, 876.

[11] Brown: Boston Med. and Surg. Jour., 1903, cxlviii, 583.

[12] Hall, J. N.: A Case of Infection by Strongyloides Intestinalis. Jour. Am. Med. Assn., 1907, xlviii, 1182.

Stiles, in discussing Price's paper, mentions four; Moore, in discussing the same paper, mentions two others; Brush,[13] three; Cline,[14] one; Daland,[15] one; Baetjer,[7] seven; Dock,[16] one; Simon,[17] five; and Patterson,‡ two. The distribution of the reported cases shows that the disease is found in nearly every one of the southern states; and some imported cases are seen in the North. The disease is far more prevalent than the number of reported cases would lead one to believe. I examined the stools of 200 students of Tulane University and found 2 per cent. of them infected with this parasite, which may be taken to indicate the prevalence among apparently healthy individuals. The prevalence among sick people must be much greater. Statistics showing the prevalence among patients at the Charity Hospital are not at hand, but the men who examine the stools, chiefly for the hookworm eggs and amebas, find the larvæ so often that they attach little importance to their presence. Mild infections are easily overlooked in the ordinary examination of the stool, since examination of several preparations is necessary. I have often noticed that, for several days at a time, a long search is required to find the larvæ in stools in which ordinarily they are easily found. I have also noticed, especially when the stools are firm, that larvæ are more numerous in the portion of the stool passed last.

THE MANNER IN WHICH LARVÆ GAIN ENTRANCE TO THE BODY

It has been proved conclusively that infection occurs both by mouth and through the skin. Wilms[18] infected a patient by feeding the larvæ, and animals can be infected in this way, although this method sometimes fails with animals (Schlüter[19]). It has been shown by Van Durme,[20] Marzocchi,§ and Daland, that the larvæ penetrate the skin and that animals can be infected in this way, and that the penetration of the skin by the larvæ causes a lesion similar to ground itch in man. In 1904 Looss[21] succeeded in infecting himself with *Strongyloides* by placing larvæ on the skin. He applied several hundred larvæ to the skin of his forearm and, on the sixty-fourth day, found the first larvæ in his stools;

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13. Brush: South. Med. Jour., 1908, i, 248.
14. Cline: Post-Graduate, 1908, xxiii, 451.
15. Daland: New York Med. Jour., 1908, lxxxvii, 761.
16. Dock: New York Med. Jour., 1909, xc, 53.
17. Simon, Sidney K.: Amebic Dysentery, Jour. Am. Med. Assn., 1909, liii, 1526.

‡Patterson, H. S.: Parasites Found in New York City, The Archives Int. Med., 1908, ii, 185.

18. Wilms: Schmidt's Jahrb., 1897, cclvi, 272.
19. Schlüter: Med. Klin., 1905, i, 1305.
20. Van Durme: Thompson Yates Lab. Rep., Liverpool, 1902, iv, 471.

§Marzocchi, V.: Gior. d. r. Accad. di med. di Torino, 1907, series 4, xiii, 3.

21. Looss, A.: Compt. rend. du 6 Cong. Internat. de Zool., Berne, 1905, p. 225.

larvæ were present on all subsequent examinations, as many as two or three in every 4 c.mm. of the feces. His conclusions are as follows:

> For the species of the genera *Ankylostoma* and *Strongyloides* there is a possible mode of entrance through the skin in addition to that by way of the mouth, by which the mature larvæ can make their way into their host. The larvæ, after boring into the skin, penetrate the superficial lymph-vessels or veins and are carried through the heart into the lungs in that way. In the lungs they pass from the blood-vessels into the air-tubes and finally wander through the trachea, larynx and esophagus to the intestines. In the lymph-glands apparently a number of larvæ are kept back and rendered harmless. The larvæ get to their goal all the more easily and in larger numbers, the younger the affected individual of the species of host. In old hosts a larger or smaller number of larvæ are kept back in the tissues where they wander around under the skin producing the skin disease known as the "creeping eruption," etc. They are able to live as long in the form of wandering larvæ as the adult worm; that is to say, about five years.

It is difficult to say which is the more common mode of infection. The frequent occurrence of strongyloides larvæ in the stools of patients suffering from amebic dysentery might be taken to indicate that infection by way of the mouth is the usual one. But, since they do easily penetrate the skin and reach the intestines and are sometimes found in patients who also have hookworm disease, it seems likely that infection through the skin is a common, if not the usual, manner of infection, as it is in hookworm disease, and that some of the ground-itch in the South is due to the penetration of the skin by strongyloides larvæ.

DURATION OF INFECTION

It is impossible to tell accurately how long man harbors this parasite, but patients are known to have had larvæ in the stools for several years. From the enormous number of larvæ in some cases it seems that these patients must reinfect themselves. It has been suggested by Grassi,[22] and later by Ward,[23] that the direct transformation of rhabditiform larvæ into filariform larvæ and then back to the parasitic mother worms may occur inside the intestine. The finding of three filariform larvæ in a fresh stool from one of my cases would seem to bear this out, but this cannot be a common occurrence, or at autopsy there would be found all the stages between the filariform larvæ and the adult worm, which is not the case.

The finding of larvæ in the sputum in Case 1 here reported, after the patient had been in bed two months, indicates that he was reinfecting himself. Because of his personal filthiness and the irritation of the skin over his buttocks and back, I thought that the larvæ were gaining entrance through the skin at this place, and probably some did. However, the presence of larvæ in the lymph-spaces and lymph-vessels of the intestinal wall suggests another plausible explanation—that the larvæ pierce the intestinal walls, enter the lymph-stream, pass up the thoracic duct into the subclavian vein, thence through the right heart to the lungs, appear in the sputum and, when swallowed, develop into adult parasites. This idea is strengthened by the fact that some of the larvæ in the sputum were young, as shown by the presence of the sexual anlage. In this way a vicious circle is set up and the infection grows steadily worse, and, as the number of worms in the intestine increases, more larvæ penetrate the intestinal walls and pass over the route above described. This must be a slow process and extend over many years, since there were comparatively few larvæ in the sections of the intestine and in the sputum, and this was a severe case as to stools.

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[22] Grassi: Gior. di r. Accad. di med. di Torino, 1883 series 3, xxxi, 119.

[23] Ward: Reference Handbook of Medical Sciences.

SYMPTOMS

Strongyloides intestinalis was first described in cases of Cochin-China diarrhea and was regarded as the cause. However, this point has been under discussion and the reader is referred to the articles by Thayer[4] and Strong,[5] in which the pathogenicity is fully discussed. Noc,[24] in a recent article, asserts that the diarrhea in Cochin-China is in reality amebic dysentery. Whatever the cause of the so-called Cochin-China diarrhea, there can be no doubt that *Strongyloides intestinalis* is pathogenic and is the cause of some of the diarrhea in the United States, especially in the southern states. While not all persons harboring this parasite have diarrhea, the proportion of those who do is large enough to convince physicians who see many cases that the diarrhea is due to *Strongyloides.*

During the last six months I have seen fifteen cases, and of these, in thirteen there was diarrhea more or less marked. In one case in which there was no diarrhea there was a tendency to constipation, but a small dose of cathartic caused profuse evacuations; in the other case there were so few larvæ in the stools that none could be found by the ordinary method of examination and only a few by the method described by Bass.[25] One of the thirteen with diarrhea also had amebic dysentery and so cannot be considered, which leaves twelve in which *Strongyloides intestinalis* was the only obvious cause. Many of these patients will deny having diarrhea, in fact, will say they are constipated; but further questioning will bring out the fact that they have periods lasting a day or two, when the stools are soft, unformed, even fluid, and of increased frequency. In the interval the stools are normal or there is constipation. This has been my experience with the university students whose stools contained the larvæ.

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[24] Noc: Ann. de l'Inst. Pasteur, 1909, xxiii, 177.

[25] Bass, C. C.: Mild Uncinaria Infections, The Archives Int. Med., 1909. iii, 446.

The severity of the symptoms is not always in proportion to the number of larvæ present in the stools. One of my patients presenting no diarrhea at all had many times more larvæ in the stools than had others presenting a moderate diarrhea.

The diarrhea is chronic and intermittent and often very suggestive of amebic dysentery. The attacks occur from once every few days to once a month, and last one or two days; in severe cases the diarrhea may be almost continuous. Usually there is no pain. The desire to go to stool is often sudden and very urgent, even when the stools are of normal consistency and this sometimes may amount to incontinence. As a rule more stools, two or three or more, depending on the severity of the symptoms, are passed during the early morning hours than during the rest of the day. The stools are very seldom dysenteric in character, unless associated with amebas, and in mild cases are not even fluid. Except in severe cases the general condition of the patient is not greatly affected; however, while none of the students harboring the parasite considered themselves ill, all were poorly nourished and anemic-looking individuals.

All of my patients had a mild anemia, the hemoglobin ranging from 70 to 90. The highest eosinophil count was 13.2 per cent., the lowest 2.5 per cent. There is usually a mild eosinophilia, although this may be absent. Sometimes a marked eosinophilia is present. Eustis, in the report previously cited, records a case showing 56 per cent.; Baetjer's case showed 45 per cent., and Daland's case 38.2 per cent.

TREATMENT

Opinions differ as to the value of treatment, for while some report successful results, the majority report failures. Eustis, in the above paper, reports a cure and attributes his success in part to the soluble diet given. On the other hand, Cline treated a patient for several months and, while the number of larvæ diminished, they did not disappear entirely. His patient received the following treatment: large doses of thymol preceded by a twenty-four hour fast, one dose per week for six weeks; bismuth-beta-naphthol daily for six weeks, except on the days thymol was administered; male-fern for two days in succession each week for six weeks; large doses of calomel and santonin for three days, followed by castor oil for three weeks. In addition he took at different times phenyl salicylate (salol) and castor oil equal parts, 60 cg., three times a day; mineral acids, iron and strychnin. Regulation of diet.

The ipecac treatment, as used in amebic dysentery, was tried in one case by Simon,[26] of New Orleans, but was not effective. In none of my cases was treatment administered. Since the infection is so common it is worth while trying various drugs in the hope that an effective one may be found.

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[26] Simon: Personal communication.

The reinfection described here easily accounts for the failure to get rid of the parasites. Larvæ which had penetrated the intestinal walls would not be affected by an anthelmintic, and on again reaching the intestines would develop into adults, so in a short time larvæ would appear in the stools even though all the adults were killed at the time the anthelmintic was administered. The treatment indicated is comparable to that for malaria; it should be repeated at intervals for a long time in order to kill those parasites which were beyond the reach of any single course of treatment.

I wish to express my gratitude to Dr. Dock, at whose suggestion I began this work, and who directed my work throughout; I wish to thank him especially for his valuable assistance in reviewing the recent literature.

I am also deeply indebted to Dr. C. W. Duval for the use of his laboratory and many valuable suggestions.

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